A Reference Handbook

OF

THE MEDICAL SCIENCES

EMBRACING THE ENTIRE RANGE OF

SCIENTIFIC AND PRACTICAL MEDICINE

AND

ALLIED SCIENCE

BY VARIOUS WRITERS

A NEW EDITION, COMPLETELY REVISED AND REWRITTEN

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NEW YORK CITY

385104
24.9.40

VOLUME VIII

ILLUSTRATED BY CHROMOLITHOGRAPHS AND FOUR HUNDRED AND THIRTY-FIVE HALF-TONE AND WOOD ENGRAVINGS

NEW YORK
WILLIAM WOOD AND COMPANY
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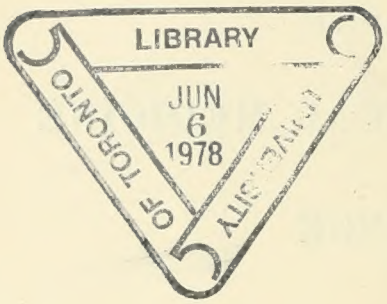

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PUBLISHERS' PRINTING COMPANY
32 AND 34 LAFAYETTE PLACE, NEW YORK

EDITORIAL NOTE.

THE last volume of the new edition of the REFERENCE HANDBOOK having now been completed, it becomes a pleasant duty to acknowledge my indebtedness to those who have been associated with me and who have done so much to bring this great undertaking to a successful conclusion. The number and nature of the articles contributed by each of them may be learned from the List of Authors and their Contributions, which is published at the end of the present volume. This list, however, conveys only an imperfect idea of the amount of time and labor which some of these writers have bestowed upon their tasks. Indeed, only those who have themselves done work of equal magnitude can form a correct estimate of the credit which belongs to each one of the men and women whose names appear in this list. Whatever usefulness the HANDBOOK possesses as a whole is due to the intrinsic value of its component parts. If a large proportion of these articles were not of a high order of merit the HANDBOOK as a whole would not have met with the appreciative reception which has been accorded to it by the medical profession of the United States and Canada, and I must in fairness state that a great deal of the credit for the organization of this mass of useful information belongs to my associates; the major part to the Department Advisers, a list of whose names appears at the beginning of Vol. I. While all of these gentlemen took, in the beginning of the enterprise, an active part in the selection of topics and of the individuals best fitted to write authoritatively upon them, a few of their number have continued to give me most efficient aid throughout the entire progress of the work. I refer particularly to Aldred S. Warthin, of Ann Arbor, Mich., Edward O. Otis, W. T. Councilman and Henry R. Stedman, of Boston, Mass., John Green, of St. Louis, Mo., Col. Charles Smart, U. S. Army, and Henry H. Rusby, William H. Park, George T. Jackson, and Robert Lewis, Jr., of New York. I am also under obligation to many of the contributors for undertaking, at short notice, work which had originally been assigned to other writers, who, owing to illness or for other reasons, had been obliged to abandon their tasks. I should be glad to mention the names of all of these gentlemen did space permit me to do so.

The elaborate and carefully prepared general index is the work of Dr. R. J. E. Scott, of this city.

A. H. B.

NEW YORK, February 1st, 1904.

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UMBELLIFERÆ.—(*The Parsley Family.*) This large family, of nearly two hundred and fifty genera and at least fifteen hundred species, is distinguished for its aromatic properties. Elsewhere in this work we have discussed the drugs ammoniac, angelica, anise, asafœtida, caraway, carrot, conium, coriander, fennel, sumbul, etc., besides certain poisonous species in a separate article on poisonous plants. These drugs have been selected for individual treatment, not because they are more efficacious than many others in the family, but because custom has given them a more permanent position in medicine and commerce. What has been written of the constituents and properties of those drugs agrees, in general, with the facts regarding all others in the family. The so-called constituents are volatile oils, oleoresins, and gum-resins, but the active portions are in almost every case the volatile oils, the resins, in a few cases only, possessing activity. Their properties incline more toward antispasmodic and carminative than toward antiseptic or expectorant effects, and they are specially valued for their pleasant aromas and flavors.

Of *Parsley* (*Apium Petroselinum* L.) both the root and the fruit are quite largely employed. The former, as it occurs dried, in commerce, closely resembles a carrot in form and size, except that it is usually split longitudinally into quarters. It is of a light orange-yellow color and somewhat annulate externally, and pale-yellow internally, with a dark zone of resin tissue near the centre. It is usually rather tough and elastic, but becomes brittle when very dry. It is fragrant and of a pungent and sweetish taste. Besides the uses named above, it has considerable repute, mostly unprofessional, as a genito-urinary stimulant. The oil of this fruit contains *apiol* ($C_{12}H_{14}C_4$) in larger quantity than does that from other parts. Pure apiol is a white crystalline body, but that usually sold is in the form of a yellowish-green thick liquid. Its special use is as a stimulating emmenagogue, in doses of 0.2–0.5 gm. (gr. iij.–viij.). Parsley oil is given in doses about twice as large, and the root and fruit in doses of from 1 to 4 gm. (gr. xv.–lx.).

Celery fruit (*Apium graveolens* L.) is closely related to parsley, resembles the fruit of the latter, has similar properties, though less active, and is used in about the same doses. Probably its chief repute depends upon the very extensive advertising of proprietary preparations bearing its name, but not of its nature.

Thapsia, or *False Turpeth Root*, is the dried root of *Thapsia Garganica* L., a tall perennial of the Mediterranean region. Sometimes the entire root is used, sometimes only the very thick fleshy bark. It contains a highly irritant yellow oleoresin on which its properties depend. Its use has been revived from time to time for its counter-irritant effects, being either rubefacient or vesicant, according to the method of application. As an emetic poison it acts very much like mustard, though it is more active, and in large doses it is a violent irritant cathartic. As a rubefacient, a plaster is commonly employed containing five per cent. of its resin, combined with turpentine, Burgundy pitch, wax, etc.

We cannot do better than to conclude by reprinting the classification of the drugs of the family published in the preceding edition of this work.

First Group.—Yielding agreeable, or not offensive, oils from their fruits (which are mostly the parts used); stems and roots sometimes eaten, often fragrant and slightly resinous; generally, European species growing in open dry places, long cultivated, and not poisonous. The most typical examples are highest on the list.

Name.	*Constituents (oils and stearoptenes).*
Anise	Fluid an[illegible] solid anethol.
Fennel	Hydrocarbon and anethol.
Caraway	Hydrocarbon (cymene) and carvol (liquid).
Ajowan	Hydrocarbon and thymol (crystl.).
Coriander	Two oils, probably hydrates of $C_{10}H_{16}$.
Cumin	Two oils, "cymol" and "cuminol."
Dill	Anethol and carvol.
Parsnip	Essential oil and inert soft[illegible] substances.
Celery	Essential oil and apiin (an inert glucoside).
Parsley	Oil and cryst. stearoptene, apiin, and apiol.
Imperatoria	Oil, [illegible]
Carrot	Oil, coloring matter (carotin).
Angelica	Oil, angelic acid, resin (has colored juices).
Lovage	Oil, resin (has colored juice).
	Etc., etc.

Various species of Eryngium and Sanicula have similar properties and uses.

Second Group.—Large Persian or African plants, with milky juice, yielding gum-resins from their stems and roots, usually offensive.

Name.	*Constituents.*
Asafœtida	Resin, gum, sulphureted oil.
Opopanax	Resin, gum, oil.
Sumbul	Resin, bluish oil.
Galbanum	Resin, gum, oil.
Ammoniac	Resin, gum, oil.
Thapsia Europæum	Irritating resin and oil
	Etc. See Asafœtida.

Third Group.—Plants containing poisonous, bitter, or nauseous principles, sometimes alkaloids of the coniine type, not usually very fragrant, sometimes without *vittæ*.

Conium (hemlock)	Alkaloids, coniine, conhydrine.
Cicuta	Cicutoxin, neutral (?) poisonous.
Hydrocotyle	"Vellarin," qualities indefinite.

Besides these, various species of *Œnanthe*, *Phellandrium*, *Sium*, and others have more or less deleterious qualities. *Henry H. Rusby.*

UMBILICAL CORD.—A knowledge of the development of the cord is prerequisite for understanding its structure at birth. Consequently its embryology will be described first, then its general condition at term, and finally the finer structure of its component parts.

EMBRYOLOGY.—In young human embryos the layer of cells which later forms the skin does not encircle the body. After covering the dorsal and lateral body walls this layer turns upon itself, and over the back of the embryo it meets and joins the corresponding layer from the opposite side, thus forming a closed transparent sac, the

amnion (Fig. 4827, *Am.*). Since the body wall is thus lacking on the ventral side, the intestinal tract is allowed to protrude. A great dilatation of the primitive intestine, the yolk sac, projects through this ventral opening

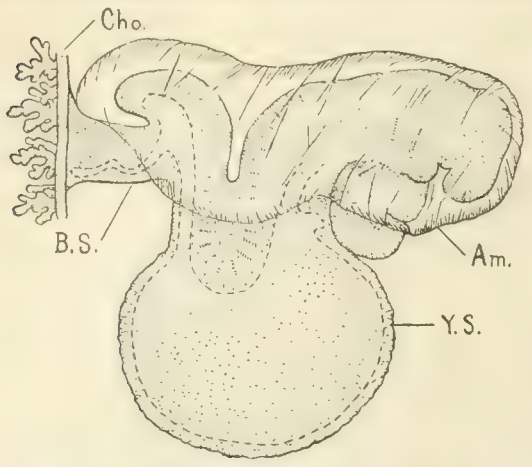

FIG. 4827.—Diagram of a Human Embryo 2.15 mm. Long. A part of the entodermal tract is shown by dotted lines. *Am.*, Amnion; *B.S.*, body stalk; *Cho.*, chorion; *Y.S.*, yolk sac. (After W. His.)

bounded by the line where the body wall is reflected to form the amnion. The yolk sac (Fig. 4827, *Y.S.*) is surrounded by an extension of the body cavity or cœlom. The entire embryo, including the amnion, lies within a hollow sphere of tissue lined with mesoderm and covered with villous ectoderm. This is the chorion, a small fragment of which is drawn in Fig. 4827 (*Cho.*). As made known by His, the human embryo is never free from the chorion, but is attached to it by a posterior continuation of the body, named the body stalk (Fig. 4827, *B.S.*). If a cross section of Fig. 4827 were made, passing between the letters *C* of *Cho* and *B* of *B.S.*, the body stalk would appear as in Fig. 4828. On its dorsal surface is the layer of ectoderm reflected to form the amnion. The ectoderm has a median depression considered by His to be a continuation of the medullary groove. The bulk of the body stalk is composed of mesoderm, in which runs a tubular extension of the intestinal tract, the allantois. This is shown in lengthwise view by dotted lines in Fig. 4827, and in cross section in Fig. 4828. The mesoderm of the stalk contains at this stage two arteries and two veins, known as the allantoic or umbilical vessels. They are constantly arranged as in Fig. 4829. The arteries pass from the iliac portion of the aorta along the body stalk to the chorion, into the villi of which they send branches. The veins convey the chorionic blood back to the embryo, passing through body stalk and body walls to the liver.

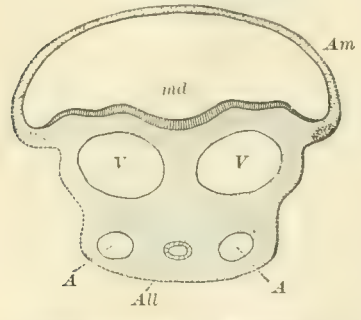

FIG. 4828. Diagram of a Cross Section of the Body Stalk of a Human Embryo. *md*, Medullary groove; *Am.* amnion; V, umbilical vein; *A*, umbilical artery; *All*, allantois.

In mammals generally, the body stalk in earliest stages is a mass of mesoderm covered by ectoderm found at the posterior end of the embryo. The entodermal prolongation then extends into the mesodermal part, and the body stalk becomes split into two portions: one consisting of ectoderm and mesoderm, and extending between amnion and body wall; the other consisting of mesoderm and entoderm, and now lying free in the chorionic cavity. The latter is the allantois. It acquires, in most mammals, an expanded terminal portion, in pigs, for example, becoming a vesicle several inches long. The allantois may then become adherent to the chorion, so that the allantoic vessels pass over into the chorionic tissue. The primates and Tarsius differ from other mammals in that the allantois is never separated from the body stalk; its cavity remains a slender tube, called the *allantoic duct*; and its connection with the chorion is never severed.

The human placenta is therefore early and elaborately developed; the allantois may be considered rudimentary.

A later stage in the formation of the cord is shown in Fig. 4829. The body stalk, instead of extending backward, now runs almost vertically. The yolk sac has become relatively slender toward its intestinal attachment, the narrow portion forming the yolk stalk. The body walls have closed in around the yolk stalk, leaving a relatively smaller ventral opening. The ectoderm over the body stalk has swung forward on both sides, and anteriorly to the yolk stalk the folds have met and united. The resulting relations are seen in cross section in Fig. 4830, *A*, which would extend from × to × in Fig. 4829. The yolk stalk now lies in a part of the cœlom that is lined with mesoderm, and is covered with that ectoderm which passes around the body stalk. The single umbilical vein is due to the early fusion of the two vessels which occurs just outside of the body. It takes place in most mammals, but not in the horse (Bonnet). In man, rarely the two veins remain apart. The umbilical arteries sometimes fuse as reported by Hyrtl—a very uncommon occurrence.

The further development of the cord is chiefly a lengthening process, due to the drawing away of the embryo from the line of reflection of the body wall to form the amnion. The yolk stalk and allantois are stretched out into very slender tubes (Fig. 4831). The yolk sac remains between the amnion and the chorion. A cross section of a later stage is found in Fig. 4830, *B*. The cœlom has become quite small. It contains, at *Y*, a mass of mesoderm, from which the entodermal yolk stalk, and the blood-vessels which accompanied it, have entirely disappeared. Bridges of mesoderm form mesentery-like structures across the cœlom, and finally obliterate the cavity. The cord then shows no trace of the yolk stalk.

THE CORD AT BIRTH.—At birth the cord is a smooth, glistening, white or pearly, apparently twisted rope of

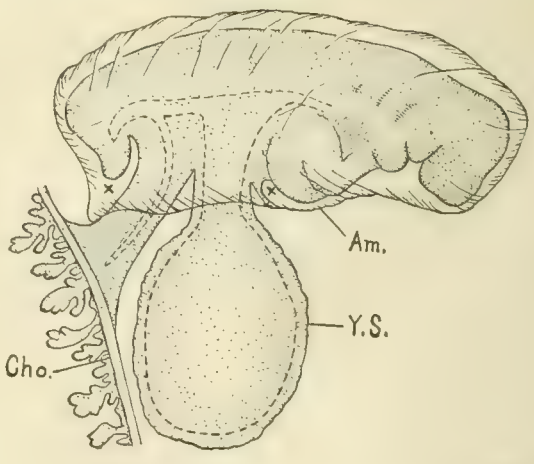

FIG. 4829.—Diagram of a Human Embryo, 2.6 mm. Long. Lettering as in Fig. 4827. (In part after W. His.)

tissue extending from fœtus to chorion. Its length is variable, but is usually about 55 cm.; the extremes are said to be 12 cm. and 167 cm., respectively. The human cord is relatively much longer than that of other

animals, a peculiarity correlated gratuitously with the great distention of the human amniotic cavity. Its diameter, also variable, averages 12 mm. The "twisting" of the cord, which begins in the second month, is generally due to the spirally arranged vessels within. They may be seen through the semitransparent substance which forms the bulk of the cord, and is called Wharton's jelly. Local thickenings in this tissue produce the so-called "false knots." Other irregularities, purplish in color, are due to intravascular blood clots. An actual twisting may occur, due to the activity of the fœtus. Thus the cord may be wound three times around the neck of the child with fatal results, or around the limbs resulting in intra-uterine amputations. Less serious entanglements are frequent. The cord may be tied in true knots, which rarely if ever interfere with circulation, since they are seldom drawn tight until birth.

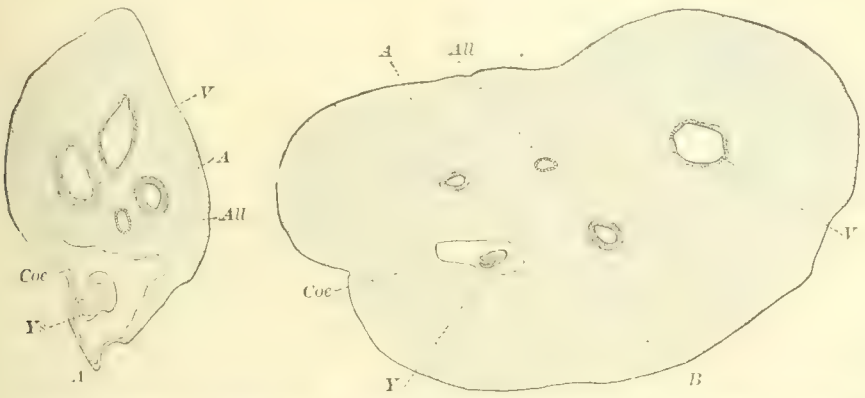

FIG. 4830.—Sections of Umbilical Cord. *A*, Embryo of 21 mm.; *B*, fœtus of sixty-four to sixty-nine days; V, Ys, yolk-stalk; *Coe*, coelom. Otherwise the lettering is that of Fig. 4828. (Minot.)

Attachments of the Cord.—The navel, or umbilicus, is the scar which marks the place of separation between the persistent and caducous portions of the cord. The persistent part is lustreless and skin-covered, differing from the rest also in possessing capillaries. Its length in man is from 7 to 9 mm. (Kölliker). The shorter it is, the deeper will be the depression at the navel, which is produced by its contraction (Virchow). In cattle it measures 2 to 4 cm., and a protuberant navel persists for some time.

At the distal end of the cord the umbilical vessels branch and enter the chorionic mesoderm. The outer covering of the cord is continuous with the amnion, which spreads out over these vessels and is in contact with the chorion. Usually the cord meets the chorion at right angles, near the centre of its placental area. Sometimes it arrives by a more acute angle at the placental margin. Occasionally the vessels reach and branch in the non-placental chorion, through which they pass to the placenta. This is the velamentous insertion. Hyrtl found eleven velamentous, nineteen marginal, fifty-four excentric, and sixteen central insertions in one hundred placentas. The velamentous form is probably due to the ovum becoming implanted with its body-stalk turned away from the decidua serotina (Peters). A rare forking of the cord has been termed the insertio furcata. (For Schultze's fold, see *Yolk Sac*).

Covering of the Cord.—The epithelium of the cord has been best described by Minot and Bowen. At two months the ectoderm is a single layer of cells; at three months (Fig. 4832) it is two-layered, the outer being a continuation of the epitrichial layer of the skin; at five and six months the epitrichium is partly cast off, and the deeper layer has become several cells thick, with its outer part cornified. Thus it is intermediate between the many-layered skin and the single-layered amnion. There are, moreover, no lines of demarcation at either end of the cord. The similarity between amniotic and umbilical epithelia is shown by the "amniotic villi" which occur on both. The cord of the cow is beset with these elevations, which in flattened form are found on the amnion. They are merely epithelial proliferations (Fig. 4833) of unknown significance. The cords of domestic animals other than ruminants are smooth. Sometimes near the placental end of human cords, and especially on the adjacent amnion extending from Schultze's fold, pinhead elevations, or larger, flat, white areas may be found. Figs. 4834 and 4835, drawn from sections of the amnion from a normal afterbirth, indicate that these structures are quite like skin. They contain a dermis of dense connective tissue, and an epidermis of germinative, granular, cornified, and epitrichial layers. The covering of the cord, which is intermediate in its structure between skin and amnion, is called skin by Minot, Foulis, McMurrich, and others, and amnion by Kölliker, Hertwig, and Kollmann.

Wharton's Jelly.—The tissue of the cord, except near the blood-vessels, is of a unique sort, known as mucous connective tissue, or Wharton's jelly. Under the epithelium, with which it is inseparably connected, it may be slightly denser. Between the three blood-vessels (Fig. 4836), the tissue is loosest and forms three indistinct columns, the chordæ funiculi. Only in an injected alcoholic specimen have these structures, described more than one hundred and twenty years ago, appeared at all conspicuous. In the meshes of the tissue is a gelatinous substance containing mucin; the meshes themselves are of white fibrous elements, together with a small and

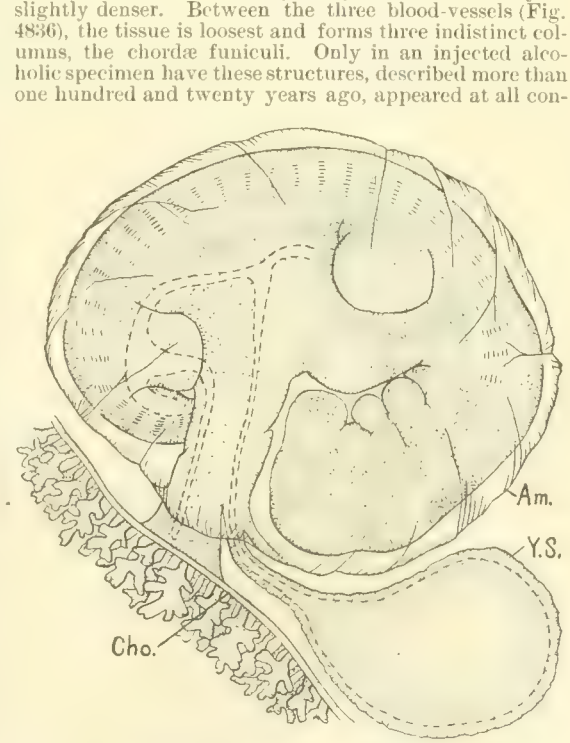

FIG. 4831.—Diagram of a Human Embryo, 7 mm. Long. Lettering as in Fig. 4829. (In part after W. His.)

variable amount of elastic tissue. The latter appears only in late stages. In a young pig embryo of 6 mm., stained by Mallory's connective-tissue method, the cord consists of a loose network of anastomosing cells between

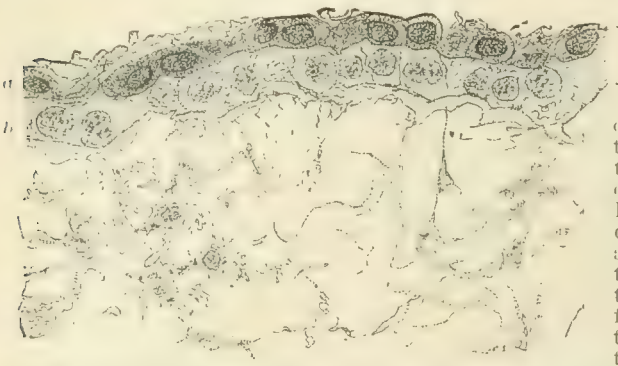

FIG. 4832.—Epithelial Covering (*Ep.*) of the Umbilical Cord of an Embryo of Three Months; *a*, its epitrichial, *b*, its inner layer. × 545 diameters. (Minot.)

which are numerous blue fibrils seeming to be quite independent of the cells (compare Fig. 4837). Kickhefel, from a study of mucous tissues, and others from general investigations, consider these fibres as transformations of cell protoplasm. Merkel and others believe them intercellular in origin. Be this as it may, the fibrils are abundant in the cord when the subcutaneous tissue shows scarcely a trace of them. In 18 mm. pigs the subcuta-

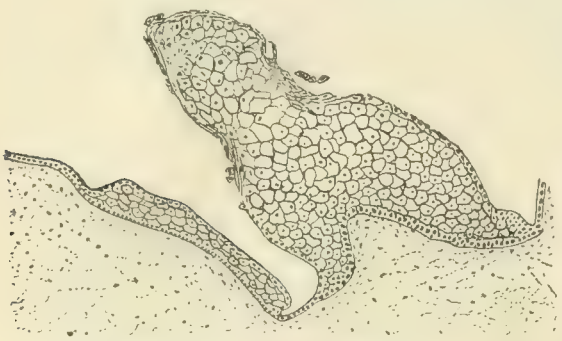

FIG. 4833.—Amniotic Villus, from the Umbilical Cord of a Fœtal Cow, 20 cm. Long. × 55 diameters.

neous tissue has many fibrils, but the cells are closer together, and their protoplasmic processes more slender and shorter than those in the cord of the same embryo. In 40 mm. pigs the contrast between the œdematous-looking cord and the relatively compact subcutaneous tissue is even greater. Free anastomosis of the protoplasmic processes characterizes the umbilical tissue throughout its development. Virchow considered that mucous connective tissue, embryonic subcutaneous tissue, and considered as a "phase" in connective-tissue differentiation, an idea inconsistent with its distinct appearance in embryos of various ages, and with the fact that it alone develops without any capillary circulation.

Blood-Vessels.—The cord contains usually two parallel arteries and one vein, all pursuing a spiral course, with the arteries winding around the vein and making, in extreme cases, forty revolutions. These may be either from left to right or *vice versa*; sometimes they are absent, or the vein is on the outside, or the arteries cross one another. Except for a quite constant anastomosis between the arteries just before reaching the chorion, these vessels are without connections or branches.

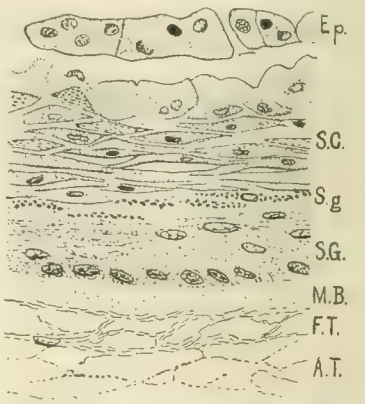

FIG. 4835.—Human Amniotic Villus. *Ep.* epitrichium; *S.C.*, stratum corneum; *S.g.* stratum granulosum; *S.G.*, stratum germinativum; *M.B.*, basement membrane of very dense fibrous tissue; *F.T.*, fibrous tissue; *A.T.*, areolar tissue. × 380 diameters.

Henneberg describes the histology of the arteries as follows: Each artery possesses an endothelium, an inner longitudinal muscle layer in which elastic tissue is abundant, but does not form a single internal elastic membrane, and an outer circular layer containing some longitudinal fibres and delicate elastic elements. The muscle cells are separated by an unusual amount of connective tissue, simulating protoplasmic bridges. There is no adventitia. The vein has an endothelium and a muscle layer, chiefly of circular fibres, but longitudinal bundles appear irregularly in this layer or on either side of it. Elastic plates are more highly developed than in the arteries. No vasa vasorum or valves exist in the umbilical vessels. Hemorrhage when the cord is severed is prevented by the contraction of the arteries, rendered possible by their lack of elastic tissue and abundance of muscle. The vein remains open, but the lumen of the artery is nearly or quite oblit-

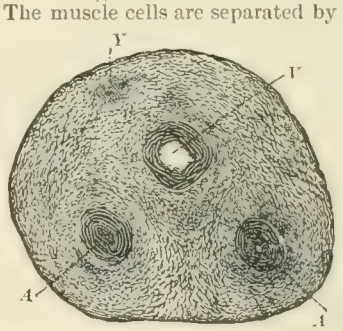

FIG. 4836.—Cross Section of an Umbilical Cord at Term. *V*, Remnant of the allantois; *V*, umbilical vein; *A*, *A*, umbilical arteries. × about 12 diameters.

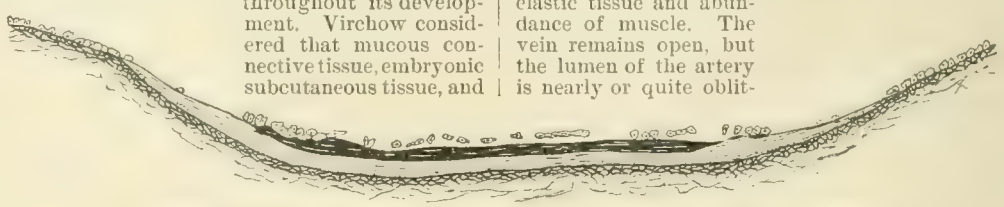

FIG. 4834.—"Amniotic Villus," from a Normal Human Amnion at Term. × 55 diameters.

the vitreous humor were quite similar, and the statement has been repeatedly copied. Since the vitreous humor has been found to be of ectodermal origin, it has recently been removed from this group. Wharton's jelly is still

erated (Fig. 4836). The stimulus causing the contraction is the tearing of the cord, which in cows accompanies the expulsion of the fœtus, in carnivora is accomplished by biting and in swine partly by trampling.

Henneberg's experiments eliminated other hypothetical factors, such as the clotting of the blood and the effect of the increased pulmonary circulation. Lochmann has recently produced general contraction of the vessels, especially of the arteries, by electric stimulation of the living cord. This is of special interest since the many attempts to demonstrate nerves in the cord have failed. Valentin is said to have traced nerve fibres from 8 to 11 cm. from the navel; other investigators have been less successful.

Lymphatics.—Various lymphatic canals, with stomata, have been reported (Tait), but these probably are merely intercellular spaces. Wandering cells are usually scattered about in Wharton's jelly. In a rare pathological specimen of the human cord, which is dotted with small white lesions resembling amniotic villi, polymorphonuclear leucocytes are abundant. The acute inflammatory process has not made evident any lymphatic vessels.

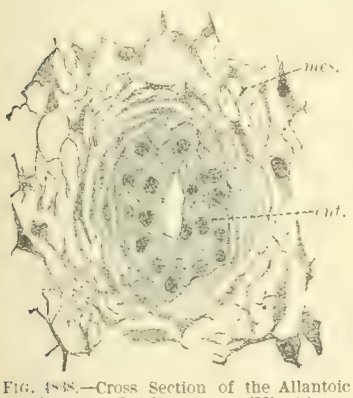

FIG. 1838.—Cross Section of the Allantoic Duct. × 340 diameters. (Minot.)

Allantois.—The allantois, as discovered by Sabine and confirmed by Ahlfeld, is generally to be found as an obliterated canal extending throughout the entire cord at birth. In earlier stages it has a lumen bounded by cuboidal cells (Fig. 1838, *cut.*). Later it is merely a strand of such cells, sometimes interrupted, but generally to be found between or equidistant from the two arteries. In the distal part of the cord its position is more variable (see Fig. 1836, *Y*). It may retain its lumen until birth, when if the intra-abdominal portion is also pervious, a urinary fistula at the umbilicus is produced. For intestinal umbilical fistula, see *Yolk Sac*.

Frederic T. Lewis

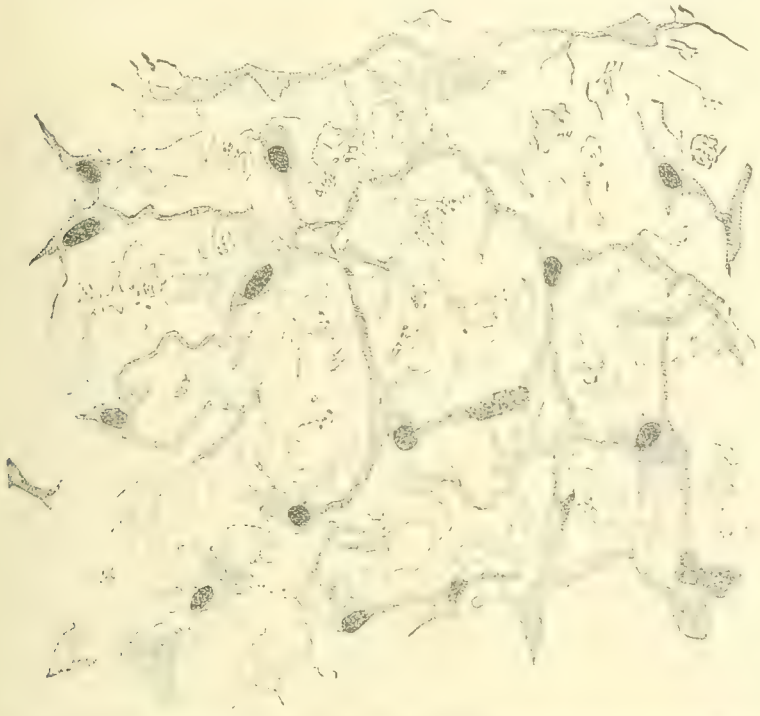
FIG. 1837.—Connective Tissue of the Umbilical Cord of a Human Embryo of about Three Months. × 511 diameters. Stained with alum cochineal and eosin. (Minot.)

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UMBILICUS, SURGICAL AFFECTIONS OF THE.—

Malformations.—Surgical interest in the umbilicus begins at birth, since there may be important congenital malformations of this part of the body. In fœtal life the vitello-intestinal duct passes through the umbilicus and connects the yolk sac, which is outside the abdomen of the fœtus, with the intestine, which is within it. Normally this duct disappears with the yolk sac at about the eighth week of fœtal life, but it may persist and give rise to a cyst at the umbilicus or a fistula lined with mucous membrane; or, if the calibre of the duct is greater, the intestine itself may be prolapsed through it, and be injured when the umbilical cord is tied at birth. Such persistence of fœtal structures will be noticed as an umbilical hernia of the cord at birth; or, if the abnormal condition is less marked, a fistula will be seen when the cord drops off a few days later. Such a fistula may or may not communicate with the lumen of the intestine. If the discharge which comes from the fistula is purely mucous in character, attempts should be made to close the opening by caustics and strapping with adhesive plaster, in order to prevent further prolapse. This treatment may succeed in curing the patient even if the discharge contains a little fæcal matter. If the faulty closure at the umbilicus is more marked, an operation may be necessary to cure the patient, which operation in its essential details is the same as that performed for the purpose of closing an artificial anus—namely, opening of the peritoneal cavity, removal of the fistula, suture of the intestine, suture of the abdominal wall. This is, of course, a serious operation for a young infant.

The edges of the duct may be everted, in which case there will be presented a red, pedunculated tumor which tends to project more and more from the umbilicus. It is covered with mucous membrane which joins the sur-

rounding skin, there being no fistula. Such a condition is easily mistaken for a granuloma, but if it is excised the peritoneal cavity will probably be opened. The condition should be treated by removal of the mucous membrane from the mass and ligation of its pedicle.

In fœtal life the urinary bladder within the abdomen of the fœtus communicates with the allantois outside of the fœtus by a duct which passes through the umbilicus and is called the urachus. If this duct persists it will be opened by the falling away of the cord and a fistula will be exposed which discharges mucus, in case only a portion of the duct is patent, and urine if the whole duct is open as far as the bladder. Cauterization and pressure will almost invariably effect a cure in these cases, provided the urine flows freely through the natural channels. This condition may be acquired in infants or children through the existence of an obstruction in the urethra, complicated by cystitis, and afterward by the development of inflammation in the remains of the urachus. The treatment in such cases is first to establish a free passage for the urine through the urethra; second, to cure the cystitis; and, third, to dissect up the urinary fistula, suture the wound in the bladder, and close the abdominal wound.

Inflammation.—In stout people the umbilical hollow is deep. If dust and secretions of the skin are allowed to collect in it, a ball of material is formed which may chafe the skin and set up ulceration or lead to the formation of an abscess. Treatment for such conditions consists in incision and drainage.

The umbilicus may become the seat of a purulent, or biliary, or urinary, or fæcal fistula, as it is the thinnest portion of the abdominal wall. The origin of the trouble may be shown by the character of the discharge; but if this is simply mucous, it may be impossible to state from what organ it comes. Diagnosis may be assisted by ingestion of food containing small solid particles—for example, huckleberries,—by irrigation of the bladder with colored fluids, etc. Treatment should, of course, be directed to the seat of the trouble.

Tumors.—The tumors which are found at the umbilicus with sufficient frequency to give practical importance to their consideration are: granuloma or fibroma, sarcoma, sebaceous and dermoid cysts, and carcinoma.

A granuloma may develop in the wound caused by the dropping off of the umbilical cord. The treatment consists in keeping the parts clean, in applying to the pedunculated mass hydrogen peroxide, carbolic acid, or some other caustic, and in carefully adjusting a gauze pad which is to be held in position by adhesive plaster. The object of these last measures is to prevent the development of umbilical hernia. A similar tumor may form in later life as a result of long-standing ulceration due to uncleanliness. Such a fibroma should be removed and the wound treated as above.

Sarcoma or fibro-sarcoma of the umbilicus is a firm tumor covered with normal skin and possessing no pedicle. It should be radically excised, and, unless the tumor is very small, it is better to open the peritoneal cavity in so doing, since the surgeon can then be more sure of cutting away all the growth.

Sebaceous cysts and dermoid cysts of the umbilicus may reach a considerable size. The proper treatment is the removal, not only of the contents, but of the cyst wall. This operation may open the peritoneal cavity.

Carcinoma, usually of the type of epithelioma, forms a shallow ulcer, with a firm base and characteristic foul-smelling secretion; or it may grow upward in a cauliflower-like mass which does not ulcerate until a later stage. The prognosis depends upon the stage at which the tumor is removed. It is rather better in sarcoma than it is in carcinoma.

Secondary carcinoma of the umbilicus occurs in some cases of cancer of the alimentary tract and female genital organs. The disease extends to the umbilicus in most cases by direct continuity. No radical treatment is possible.

Hernia.—Umbilical hernia existing at birth or developing in infancy will rarely require operation. Such a hernia is usually small, perfectly reducible, and easily controlled by a small pad held in place by adhesive plaster. A curved wooden button mould covered with gauze makes an excellent pad for this purpose. To avoid irritating the skin of the abdomen the plaster straps should be left in place several days, and each time they are changed they should be placed in a different direction; for example, first vertical, then horizontal, then oblique, etc. The new pad and strapping should be at hand before the old one is removed, and the finger of the nurse should control the hernia during the change of dressing. If this treatment is conscientiously followed, most of these herniæ will be completely cured in a few months. In older children operation is required.

Umbilical hernia in adults is a much more serious condition. It is usually complicated with adhesions, so that the hernial contents are only partly reducible. On this account the wearing of a truss is unsatisfactory and possibly dangerous. (For the operative treatment of umbilical hernia see article on *Hernia.*)

Edward Milton Foote.

UNAKA SPRINGS.—Unicoi County, Tennessee.

Post-Office.—Unaka Springs Hotel.

Access.—Viâ Southern Railroad to Johnson City, thence viâ Ohio River and Charleston railroad (Tennessee division), twenty-three miles to Unaka Springs.

The location is seventeen miles from Jonesboro. This resort is pleasantly located in a small cove, containing eight or ten acres, at the foot of the Unaka Mountains. The location is about 2,000 feet above the sea level, and is entirely surrounded by higher elevations. The springs are four in number and flow about 9,000 gallons per hour. No analysis has been made. The waters are said to contain iron and sulphate of magnesia. They are recommended for indigestion, chronic dysentery, and other diseases.

James K. Crook.

UNDERWOOD SPRING.—Cumberland County, Maine.

Post-Office.—Falmouth Foreside.

This spring is located on the shores of Casco Bay. It yields about 200,000 gallons of water per day, and is said to have been used by white men since the days of Weymouth, the English explorer. The following recent analysis was made by a chemist whose name we have been unable to secure: One United States gallon contains (solids): Sodium chloride, gr. 0.86; silica, gr. 0.50; calcium carbonate, gr. 0.48; magnesium carbonate, gr. 0.14; potassium sulphate, gr. 0.12; organic matter, none. Total, 2.10 grains.

The water is used commercially. Being lightly mineralized and entirely free from organic matter, it is well adapted for table use. It is also said to be useful in conditions due to the uric-acid diathesis, gall-stones, urinary irritation, gout, rheumatism, and dyspepsia.

James K. Crook.

UNICORN ROOT. See *Aletris.*

UPPER RED BOILING SPRINGS.*—Macon County, Tennessee.

Post-Office.—Red Boiling Springs. Hotel.

Access.—Viâ Nashville and Chattanooga Railroad to Carthage; thence twenty-five miles by stage to springs. Or viâ Louisville and Nashville Railroad to Gallatin, thence forty-five miles by stage. Or viâ Middle and East Tennessee Central Railroad to Hartsville; thence twenty-eight miles by stage.

This resort was formerly known as Whitley Springs, and for many years its waters have had a wide reputation in this section. They are located on the highland rim in the eastern part of Macon County, a region well known for its fine climate and beautiful scenery. The Red Spring throws up a large amount of gas, which gives it

* No connection with Red Boiling Springs (Vol. VI., p. 862).

the appearance of boiling. It deposits a brilliant red sediment, which covers the sides and bottom of its basin and imparts a reddish tinge to the water. The Black Spring also possesses this peculiar boiling characteristic. The Red Spring was analyzed by Messrs. J. M. Safford and J. C. Wharton in 1893, with the following results: One United States gallon contains (solids): Calcium sulphate, gr. 31.16; calcium carbonate, gr. 7.03; magnesium carbonate, gr. 5.75; sodium chloride, gr. 43.87; potassium chloride, gr. 0.44; aluminum sulphate, gr. 0.15; iron carbonate, gr. 0.10; silica, gr. 0.47; organic matter and loss, gr. 2.42. Total, 91.39 grains. Gases: Sulphureted hydrogen and carbonic acid, 9.95 cubic inches. The waters of the Red Spring are highly recommended in renal and bladder affections, especially those arising from the uric acid or lithæmic tendency. They are believed to possess a powerful solvent action on renal calculi and gravel. These waters are also said to be of great value in cases of chronic uterine inflammations, leucorrhœa, etc. The Black Spring water has an excellent reputation in the treatment of rheumatism. The waters of both springs possess tonic and appetizing qualities. A comfortable hotel, with modern conveniences and abundant bathing facilities, was built in 1890. There are also a number of private boarding-houses in the vicinity.

James K. Crook.

UPPER SODA SPRINGS.—Liskyon County, California. Hotel.

These excellent springs are situated on the line of the Shasta scenic route of the Southern Pacific Railroad, at an elevation of 2,363 feet above the sea-level. The location is in Sacramento Canyon, and is picturesquely surrounded by immense forests of pine, fir, spruce, cedar, etc. At the springs is a quiet, spacious, old-fashioned hotel with wide verandas and an air of solid, homelike comfort. The waters are of the alkaline-carbonated class and are very palatable and wholesome. They contain chlorides of sodium and potassium, carbonates and bicarbonates of sodium, magnesium, potassium, iron, calcium, sulphates of sodium and magnesium, and a large quantity of free carbonic-acid gas. The water is aperient, diuretic, tonic, and antacid. It is highly recommended in the treatment of the uric-acid diathesis, gravel, and calculi, and irritative states of bladder and kidneys. The water is also of value in acid dyspepsia and flatulence.

James K. Crook.

URÆMIA. See *Auto-Intoxications*, and *Kidneys, Diseases of*.

URÆMIA, TREATMENT OF.—Regarded from the standpoint of treatment, the term "uræmia" should cover all derangements due primarily to blood poisoning on account of deficient elimination by the kidneys. The term then would include a number of functional disorders causing more or less prolonged invalidism, as well as the more serious conditions to which it is commonly applied. To limit the term to a more definite series of changes or symptoms is not practicable, because of the great variety and diverse nature of the poisons operative in different cases. How entirely dissimilar such poisons may be is illustrated by the fact that the symptoms which follow upon acute obstructive suppression of the urine are very different from those which occur in ordinary uræmia. Death follows in such patients with scarcely one of the clinical features of the latter state. In a case of the kind which I saw in consultation, the patient had his left kidney destroyed by a calculus becoming impacted in its ureter thirteen years before. At the time of my visit he had not passed any urine whatever for eight days; a condition of affairs which warranted the belief that a calculus had become similarly impacted in his right ureter. I stated that if not relieved by operation he would die, as similar cases do, without any symptoms of ordinary uræmia; and so he did, as the operation was refused. He retained his consciousness up to the end, and did not experience convulsions, coma, dyspnœa, vomiting, or intestinal symptoms, and there were no evidences of pulmonary congestion or of œdema in any part of the body. His death was apparently due to asthenia pure and simple.

A careful study of the great variety of symptoms of uræmia itself in different patients suggests the inference that there must be a corresponding variety of distinct poisons present in them, some of which it may be possible to recognize by their own special properties, in the same manner as we would recognize any of our drug poisons by their special properties. We might expect this to be so *a priori*, because modern chemistry has demonstrated that different poisons may arise in the decomposition of even the same tissues; and that the poisons of uræmia originate in the disintegration of the tissues of the body, scarcely admits of a doubt. Thus, two distinct poisons have been isolated from nervous tissue, viz., cholin and neurin, and their presence has been detected in the cerebro-spinal fluid drawn off during life in patients with some form of disease of the nervous system of a degenerative nature. Of these two poisons, neurin is much the more virulent, and it presents properties quite different from those of cholin.

So in uræmia I believe that we have among others one special poison—viz., urea—which is commonly present and which has an important bearing upon the course of renal diseases. The presence of this poison can be distinguished by its own specific effects, and, what is more for our present purpose, it can be combated by appropriate treatment.

In all cases of acute nephritis, from the onset of the first symptoms, a remarkable change occurs in all the arteries of the body, for they shrink in size, and the pulse accordingly rises in tension. The most striking fact about this change is its subsequent persistence, for it continues as long as the nephritis continues, and should that become chronic the high tension becomes likewise established for months or years. This has led many erroneously to attribute the high-tension pulse of chronic renal disease to endarteritis, supposedly caused by the poisoned blood circulating in the vessels. But while it is true that changes in the coats of the blood-vessels, especially when they proceed to the extent of obliterating the lumen of the arterioles, will mechanically cause high-tension pulse, yet this latter symptom appears long before such changes occur, and, as we will show, it is the strain of high tension, rather than the toxic condition of the blood, which causes the endarteritis.

That the high tension is due, not to kidney disease as such, but to the presence in the blood of some special poison, is rendered probable by the opposite condition of low-tension pulse in some patients with marked accompaniments of renal derangement, such as albuminuria and œdema. In these, however, cardio-vascular changes are significantly absent, the arteries being everywhere soft and permeable and the heart unaffected.

In the other class, on the contrary, the pulse is hard and wiry and the artery, though smaller than natural, is yet easily palpable to the touch from being overfull, while in the early stages, before changes have taken place in its coats, it may feel (or be) quite smooth. Ere long the heart gives signs of overwork, from the ischæmia caused by the universal contraction of the arteries, and it becomes hypertrophied. Acute dilatation of the heart, however, may occur at this stage and be associated with very serious symptoms, although not a sign of thickening or of atheromatous change can be detected yet in the arteries accessible to examination.

We have at our command, it so happens, an agent which, when it is experimentally injected into the circulation, produces in the arteries exactly the same condition as that which we have just described. Suprarenal extract, or its active principle, adrenalin, acts as a very powerful and universal vaso-constrictor, and thus greatly raises the general arterial pressure, so that its effects are indistinguishable from those of the supposed blood poison which we find operative in nephritis. If this be a fact it is not necessary to postulate that the daily amount of

poison generated must be great to account for the high-tension pulse that persists in kidney disease for months together, because Schaffer and Oliver have shown that nothing is so extraordinary about adrenalin as the minuteness of the dose which will act on the whole vascular system, gr. $\frac{1}{8000}$ being sufficient to affect the pulse of a healthy man. If the supposed kidney poison possesses properties at all similar to those of suprarenal extract, its effect would be the same as a continued overdosing with this drug. Under its influence both arteries and arterioles throughout the body would so contract that the heart would labor against a universal obstruction, until, after first enlarging, it might suddenly dilate and fail.

Schaffer, moreover, reports, as one of the striking results of the intravenous injection of suprarenal extract, a most extraordinary shrinkage of the kidney itself, a condition which could not fail seriously to impair its excretion of urea.

It follows as a matter of course that the administration of vaso-dilators is indicated in all such conditions as we have just described, both to relieve the heart from its extra labor caused by arterial obstruction, and to restore the normal conditions in the circulation of the kidneys themselves. For this purpose the nitrites have long been employed, and with good results. The nitrites, however, in every form, even in that of the tetranitrate of erythrol, have the disadvantage of being very evanescent in their action, and the dose often requires to be much increased in order to keep up the effect. In my opinion the ideal vaso-dilator is aconite, and its administration in doses of five drops of the tincture, three or four times a day, is followed in time by the most unmistakable beneficial effect, not alone as regards the general systemic symptoms, but also in respect to the kidneys, which show a marked restoration of functional power. In this case the uncertainty which so commonly characterizes therapeutical inferences, cannot justly be imputed to the action of aconite, for under the steady administration of this remedy the daily excretion of urea increases to from twice to four times the average daily amount excreted before its administration.

I have now the records of observations made on ten patients, four in private and six in hospital practice, in whom the daily excretion of urea was first estimated for from three to six days previous to taking aconite, and then afterward for as long a time as the remedy was administered—*i.e.*, for periods varying from three weeks to nine months. In two of these patients the urea rose from 8 to 32 gm. daily; in one, from 10 to 40 gm. In one case, which I have published, the excretion rose from a daily average of 8 gm., noted for two months, to 32 gm. daily after five drops of the tincture had been given every three hours for one week. The aconite was continued for six months, and then twice diminished to half the dose. The output of urea soon fell to 14 gm., but returned to 30 on resuming the full dose. After six months the aconite was discontinued and the nitrites (tetranitrate of erythrol) were substituted. The urea again fell to 10 gm., when, the aconite being again resumed, the quantity rose to 32 gm.

The same results, so far as the excretion of urea is concerned, followed in the other nine cases. Three of those were hospital patients, and in two of them, after a month's use of aconite, the effect of omitting it altogether for three weeks was carefully noted. With each patient a week passed before the elimination of urea fell off, but then the diminution became decided. The third patient, who came into the hospital with anasarca and albuminuria, severe cerebral symptoms, and extensive cardio-vascular changes, improved so much that he refused to stay long enough for us to observe the effects of withdrawing the remedy.

Next to the improvement in the kidneys, including the disappearance of albumin and casts, the most marked effect of aconite is in relieving the cardiac oppression. In the case above alluded to, acute dilatation of the heart was the first condition which her physician found, and for two months she could not have her head raised, or even be turned in bed, without threatening symptoms of syncope. As soon as the aconite was given, it seemed to act on the heart as a restorative instead of a sedative, doubtless from the relief which the heart experienced from the removal of the general arterial obstruction.

On the other hand, I hold that the administration of such a vaso-dilator will be of the highest service in preventing the development of endarteritis, besides checking the progress of changes in the kidneys themselves; for it is well recognized that atheroma develops in the arteries at the seat of the most long-continued strain, and that is just what high tension is sure to induce.

We cannot expect much from aconite, nor from any functional vaso-dilators for that matter, in conditions in which widespread chronic endarteritis has already caused extensive obliteration of the smaller arteries. In such conditions the pulse tension, as already remarked, is due to permanent closure of a great number of peripheral vessels, and neither aconite nor any similar agent can dilate vessels which have practically ceased to exist. In cases of senile hearts, therefore, aconite should be given with discrimination. Even in them, however, should the pulse be not only of high tension, but also rapid, aconite may be advantageously given till the pulse falls to normal frequency, and then it should be intermitted; for I have seen it do much good in old people who, from their quickened pulse, appeared to have some acute exacerbation of chronic renal trouble.

In puerperal eclampsia we have a remarkable illustration of such a poison being rapidly formed and giving rise to extreme high tension. But, in addition to this high tension, we have the most dangerous addition of another element, viz., the rapid and powerful action of the heart itself. Schaffer's experiments with intravenous injection of suprarenal extract supply a striking parallelism to this condition, for he found that if, after the suprarenal extract had been injected, the vagi were paralyzed with atropine, the heart then acted very violently and forced such an increased amount of blood into the contracted arteries that an enormous rise in blood pressure followed. Under these circumstances the excessive intracranial vascular tension is likely to give rise to a fatal status epilepticus unless the pressure be promptly relieved. It would seem, therefore, that in puerperal eclampsia an analogous paralysis of the vagus occurs, either by overstimulation, by an excessive generation of the vaso-constrictor poison, or else by the conjoint action of this and some other poison resembling atropine. This surmise cannot be considered improbable, if the varied nature of the poisons of uræmia are considered.

Clinically, the best and speediest vaso-dilator which we can use to relieve such a condition is free venesection; but, if that be objected to, then veratrum viride should be given in very large doses, administered according to the effect which it produces on the tension of the pulse, but without reference to any other consideration. Aconite is much too slow for such an emergency, and, besides, aconite does not have the specific effect of veratrum on the great splanchnic blood-vessels. Our object is to quiet the heart and relax the arteries by bleeding the patient, as has been expressed, into her own abdominal veins, which when fully relaxed can hold all the blood of the body.

Precisely the same kind of convulsions as those which take place in puerperal eclampsia occur in acute alcoholism in men, and they have to be treated in the same way, either by full venesection or by doses of twenty drops of the tincture of veratrum viride administered every twenty minutes till the tension of the pulse is counteracted. I have given two drachms of this tincture in four hours and a half in a case of that kind, and as a result of these heroic doses the convulsions ceased and the patient recovered.

It is too commonly the case that practitioners are content in their examinations of the urine to search for only what ought not to be there, such as blood, albumin, casts, pus, sugar, etc. Their examinations, however,

should extend also to determining whether the urine contains its normal ingredients in proper proportion and amount. Often the urine may not contain any foreign elements, and the kidneys be free from any organic disease, and yet the patient remain seriously out of health from deficient elimination of urea and other solids. Nothing could be more puzzling than the narration, which patients often make, of symptoms which, particularly as regards nervous manifestations, seem to be inconsistent with any known disease. This feature of itself should lead us to suspect a general toxæmia of some kind, and most likely either of renal or of intestinal origin. Headaches, mental depression, severe neuralgias constantly shifting from one part of the body to the other, all kinds of paræsthesiæ, somnolence alternating with insomnia, and a sense of general prostration, especially in the morning, and also in some instances morning polyuria, are among the many symptoms of which such patients are likely to complain. The diagnosis of the condition is at once made clear when a proper examination of a specimen of the collected urine for twenty-four hours is made, and the output of urea is found to be only one-fifth, one-third, or one-half of what it ought to be for persons of their age or weight. The elimination of urea ought to range, for a woman in good health, between 18 and 20 gm., but it is singular how long some women will live eliminating only 10 gm., or 5 gm., or even only 4 gm., daily for months together. Hysteria is the commonest verdict pronounced upon them, owing to their ever-changing nervous symptoms. But I have had, among men, a number of patients who manifested just such symptoms, both in kind and in number, and in them I have found the urea output to amount to from 11 to 15 gm., when it should range from 22 to 30 gm. Neurasthenia is the favorite term applied to cases of this nature.

In all such patients the pulse tension is low, and there can be little doubt that the underlying disorder, whatever it may be, differs materially, both etiologically and pathologically, from that which is present when the elimination of urea is low but the pulse tension high. In true hysteria I have not found the elimination of urea specially deficient. As to the other solids of the urine the records vary remarkably. Some urines with a low percentage of urea have a great excess of other solids, while in the case of others the total solids may be diminished. The chief factor, therefore, is deficiency of urea. My own view of the etiology of these disorders is that they are of gastro-intestinal origin. In health there is a significant association between the intake of food and the elimination of urea by the kidneys. Within the first hour after a full meal the elimination of urea is from twice to three times what it will be in the fourth hour after the meal. That fact seems to explain why attacks of apoplexy so commonly follow Christmas or Thanksgiving dinners in those who have already damaged kidneys. The serious effects, in kidney diseases, of errors of diet are a further evidence of the close relation of the gastro-intestinal tract to the renal functions. It seems to me, therefore, quite conceivable that certain disordered states in the alimentary canal may exert an inhibitory effect, so to speak, upon the elimination of an adequate amount of urea by the kidneys. At any rate, instead of aconite or vasodilators being of any service, I have found the restoration of the normal output of urea best secured by a persevering and systematic use of intestinal antiseptics. A weekly, or bi-weekly, dose of blue pill is very efficacious. On rising in the morning the patient should take a drachm and a half of sodium sulphate, or of sodium phosphate with ten grains of sodium salicylate, dissolved in a tumbler of water as hot as he can sip. The benzoates are also of much service. Ten grains of either the sodium or the ammonium benzoate may be mentioned as the proper dose. Three such doses, either with or without an equal amount of sodium salicylate, are commonly taken (the benzoate and the salicylate in two separate capsules) in the course of the day—one about an hour after each of the first two meals, and the third just before retiring for the night. Some physicians prescribe, in preference to the above, a mixture of castor oil (ɱ xv.) and salol (gr. v.), to be taken half an hour after each meal and again at bedtime. Each dose is enclosed in one of Starr's shellac-covered capsules. Red meats should be avoided, especially at night, and among vegetables asparagus and beets.

The treatment of uræmia occurring in organic derangements of the kidneys is treated fully elsewhere (Vol. V., p. 343), and, therefore, I will only allude to some particular conditions. In acute scarlatinal nephritis, the first danger signal from the kidneys is not the appearance of albumin or of blood corpuscles under the microscope, but a diminution in the quantity of urine excreted and a fall in the specific gravity. When a discovery of this kind is made, treatment should be begun at once. One of the most effective measures that can be employed under these circumstances is the rectal douche, with normal saline solution at 115°–120° F.

Action of the bowels always causes a flow of urine in health, owing to the nervous association between these two adjacent viscera; and this association stands us in excellent stead whenever the kidneys are, from any cause, failing to secrete. I would place more reliance upon this one than upon any other single measure in scarlatinal suppression of urine. At least two gallons of the hot saline solution should be allowed to run in and out at a time, the best instrument for which purpose that I know of being Kemp's rectal irrigator. (See article on *Enteroclysis* in Vol. III.) I have seen also most excellent results from hypodermoclysis in these cases and in the hemorrhagic nephritis of diphtheria. In such cases it is well to inject, beneath the skin of the flank, from two to four ounces of normal saline solution. (See article on *Hypodermoclysis* in Vol. IV.) We need hardly despair of even the most seemingly desperate case of scarlatinal suppression; and if deep coma supervenes, I have found effectual a procedure recommended by Brown-Séquard; it consists in dipping a tablespoon in hot water and holding it in contact with the skin over the kidneys until the surface shows signs of being scalded.

With reference to some points connected with the treatment of chronic interstitial nephritis, I may state that it is not uncommon for a person to be suddenly taken with uræmic convulsions as the first announcement to anybody that he has Bright's disease. Post mortem we find that such persons have long been carrying diseased kidneys with them, with only moderate accompanying symptoms, which they had accredited to biliousness, etc. Others, on the contrary, have long been known to have kidney disease, but they have got along fairly well for many months, or they have even attended to business, and then suddenly serious symptoms have developed and the disease has soon carried them off.

I believe that in the great majority of such patients there has entered into the case a new element, the recognition of which we owe to recent advances in pathology; I refer to a septic invasion of the kidneys by bacteria, of which the commonest form is the colon bacillus. Dr. Flexner has been one of the foremost investigators who have demonstrated the rôle which terminal infections play in the final issue by death of many chronic diseases, particularly diseases of the heart and of the kidneys.

In chronic interstitial nephritis the process seems to be this: A patient with cirrhosed kidneys, who has had polyuria for months, begins to pass much less urine, or perhaps very little. He is then beginning with virtually the same conditions as those which are present in a case of commencing scarlatinal nephritis. Soon afterward he has a convulsion, and becomes comatose, or he has, during the night, an attack of uræmic asthma with œdema of the lungs and pleural effusion, or an attack of vomiting and diarrhœa. Often thereafter the kidneys stop secreting altogether and death follows. At the autopsy the kidneys are found to be acutely inflamed, stuffed with micro-organisms of various kinds, but most frequently with the colon bacillus.

There is nothing so much to be dreaded as an attack of so-called cholera morbus in an elderly person. In such a case we should at once turn our attention to the kidneys, to find out what their condition is. Something also of this kind undoubtedly occurs in those cases which heretofore have been regarded as simply an acute exacerbation of the original chronic malady. I think that I have repeatedly, in patients whose kidneys were in a cirrhosed condition, warded off the worst results after threatening symptoms, such as fever, mental clouding, Cheyne-Stokes breathing, vomiting, and the like, had manifested themselves, by the prompt administration of mercurial cathartics, followed every two or three hours by ten grains of urotropin combined with ten grains of sodium benzoate. In my experience urotropin does not cause untoward symptoms if sodium benzoate is given along with it. Of course, hot saline rectal irrigation also should be used, as in a case of scarlatinal suppression. Against the presence of the colon bacillus in the kidneys urotropin is at least as much of a specific as it is against the bacillus typhosus.

In all cases of chronic interstitial nephritis our prognosis must always be uncertain, because we can never be sure how much working kidney substance these patients may still have. Not uncommonly the most unlooked-for improvement in the action of the kidneys will occur, and then continue until it is suddenly cut short by some error of diet, such as a too hearty meal of meat, particularly if taken at night. With reference to this point we may remark that there is an apparent difference in the activity of proteid metabolism between the day and the night hours. We have a whole series of affections, marked chiefly by nervous disturbances, which are evidently due to various toxæmias, and which are all characterized by being worse in the early morning hours. Many cases of melancholia and of migraine, and all cases of Graves' disease show this peculiarity. In Graves' disease the twenty-eight symptoms, aside from the goitre and exophthalmos, which I have found to be characteristic of this singular malady, are, without exception, worse in the morning. In my notes I have records of no less than eight who could not write or sew in the morning, but could do so in the evening. In all such cases of melancholia, migraine, or Graves' disease, I enjoin entire absence from red meats, especially beef, and most of all at night. Then again the first attacks of gout and of peptic asthma always occur after midnight. I have repeatedly noticed that many patients can take beef at breakfast or at lunch, but if they take it at evening dinner it is sure to cause a very troubled sleep. All these particulars should be borne in mind when we aim to regulate the life of a man who comes to us with a high-tension pulse and rigid arteries.

The chemistry of these night-generated poisons is yet to be worked out, but there can be no doubt that they have much to do with changes which take place in the alimentary canal, changes connected with the nitrogenous elements of food, particularly the red meats; and every person with cirrhosed kidneys should be enjoined, like an asthmatic, not to eat heartily after midday.

For the rest, I may say that the greatest remedy for auto-infection and the best prophylactic against the manifold dangers of chronic interstitial nephritis is life in the open air. Such a case needs a milder climate in winter, just as much as any bronchitic or phthisical patient does. Intestinal antiseptics are of the greatest value; and, as to special medicinal remedies, I have great faith in the employment of gr. $\frac{1}{2\frac{1}{2}}$ of bichloride of mercury, t.i.d. for one week out of three weeks, and of small doses (not more than five grains) of sodium iodide t.i.d., to be taken for prolonged periods.

There can scarcely be a stronger contrast than that which exists between the clinical features of a typical case of chronic interstitial nephritis and those of an equally typical case of chronic parenchymatous nephritis. The first is most commonly a disease of middle or of past middle life, and is associated with the changes of advancing years. Parenchymatous nephritis, on the other hand, attacks the young oftener than the aged, and is not infrequent among children. In kidney cirrhosis albuminuria is usually insignificant in amount, repeatedly is absent, and at no time is of much import as such. In parenchymatous nephritis albuminuria is steadily present and abundant. But, above all, in interstitial nephritis the patient is never waterlogged, unless from consecutive heart disease. In parenchymatous nephritis there is from the beginning a tendency to a general leakage of water into the tissues, so that it often appears first in the face instead of the feet, and the mechanism of this dropsy remains, up to the present time, wholly unexplained. Along with these conditions, anæmia occurs early and is persistent, so that in view of all these differences there can be little doubt that the systemic poisoning in the one disease is quite different in kind from that in the other.

The anatomical changes in the kidneys in these two forms of nephritis are equally contrasting. The capsule of the tough cirrhosed kidney is found to have become almost an integral part of the shrunken organ. It so dips into and adheres to the kidney substance that we have to tear away bits of this if we wish to strip off the membrane. The capsule of the large white kidney is stripped off the soft organ as readily as the rind is from an orange. It is true that these changes are not uniformly restricted to diseased kidneys of either kind, and interstitial changes may be found in parenchymatous nephritis; furthermore, kidneys which are white but not large are not uncommon. But the clinical differences still remain as marked as ever; and, moreover, in the white kidney we find conditions which readily explain why those patients are so difficult to relieve or cure. The glomeruli are pressed upon by masses of the round cells, which fairly stuff Bowman's capsules, and the tubules are choked with every kind of débris.

Now it would seem that if we only had in the kidney the double circulation of the lung, all this ruinous accumulation might be got rid of. We have interstitial pneumonia, if the lung exudates are not removed, just as we have interstitial nephritis also in the kidney if it remains clogged with inflammatory exudates; but interstitial pneumonia is rare, because in the lungs we have the double currents of the pulmonary artery and of the bronchial arteries, and between them the immense exudates of a croupous pneumonia are got rid of, usually before the stuffed air cells are damaged. In the kidneys, on the other hand, we have the one renal artery, which answers to the pulmonary artery in the lungs, and nothing more. To expect that the kidney capsule will allow enough blood-vessels to enter through it to help absorption would be even less warranted than to expect help from the blood-vessels of the pleura to assist in the removal of the inflammatory exudates in the air cells.

We seem, in this condition, to have an obstacle which wears the aspect of a mechanical obstruction quite insuperable to our ordinary medical remedial measures. The attempt to increase the outflow of watery urine by prescribing diuretics for the relief of the dropsy oftener fails than succeeds. We may temporarily succeed by trying one diuretic after another, but the cause of the dropsy remains and the œdema returns just the same as ever. All we can do, then, is to throw upon the skin and bowels the task of working vicariously for the kidneys; but in the majority of instances we make no real headway. Some patients with chronic kidney disease, with dropsy and persistent albuminuria, recover; but whether they do so on account of our therapeutics, or whether they recover spontaneously, we cannot tell.

Such conditions would suggest the advisability of having recourse to surgical measures of relief for the embarrassed renal circulation, and this subject has of late been prominently brought to the attention of the profession by Dr. George M. Edebohls, of New York. In a communication published by him in the New York *Medical Record*, March 28th, 1903, he gives reports of 51 patients, 29 females and 22 males, in whom he had performed decapsulation of the kidneys for chronic nephritis of the inter-

stitial, diffuse, and parenchymatous forms. Of these, 39 cases were more or less benefited, including 19 completely cured, none being considered cured unless they had been for six months free from any signs in the urine of diseased kidneys. For further particulars the reader should consult his paper; but there can be no doubt that this procedure was successful in a sufficient number of patients with serious renal changes to merit its extended trial by other operators.

That the beneficial result followed upon a freer circulation within the kidneys, upon the removal of the constricting capsule, there can be no doubt; but whether an additional factor exists in the development of a new supply of blood-vessels formed in the perirenal tissue after the capsule has been removed, is doubted by Dr. Harold A. Johnson, of San Francisco,[1] who decapsulated the kidneys of ten dogs and examined the kidneys at various dates after the operation. He states that a new capsule is formed about the kidneys without the development of any considerable anastomosis between the renal and the perirenal vessels. The objection to this observation is that the results of such an operation upon healthy kidneys in dogs scarcely prove that a new capsule will be formed in human subjects with kidneys so embarrassed in their circulation that new channels can be taken advantage of whenever possible, as commonly happens in hepatic cirrhosis.

In the management of a case of general renal dropsy, with abundant albuminuria, I may add that I have repeatedly observed that the kidneys start up, as it were, and carry off the water when milk and a fluid diet are given up, and solid food, including meat, given instead, with a restriction of liquids. The effects of such a change in regimen, however, should be watched carefully.

As to diaphoresis, the subcutaneous infiltration makes the skin tense and glossy, and thus closes the sweat ducts whose opening on the surface is at an angle. A thorough oiling of the skin, therefore, before using our diaphoretic measures, makes the action of the sweat glands much more effective. *William H. Thomson.*

URAL; URALIUM.—This drug is also known as *chloral-urethane,* and, as its name implies, it is a compound of urethane and chloral. It occurs as a white crystalline body, readily soluble in alcohol, but almost insoluble in water. It is decomposed by hot water.

Ural was introduced by Dr. Poppi, of Bologna, in 1889, as a better hypnotic for neurotic patients and the insane than are most of the drugs employed for this purpose. He considered it to be more active than urethane and more safe than chloral, and better borne by the stomach. In the hands of others it has not furnished such favorable results, and has not secured any position as an hypnotic remedy. *Beaumont Small.*

URANIUM ACETATE AND NITRATE, $UO_2C_2H_3O_2$-$2H_2O$ and $UO_2(HNO_3)_2.6H_2O$, are yellow crystalline salts which are soluble in water, and have been employed to some extent in diabetes in dose of 0.01–0.02 gm. (gr. $\frac{1}{6}$–$\frac{1}{4}$). It is claimed that they stimulate the sugar-consuming cells of the body. The acetate has also been used as a catarrh snuff or in solution as a nasal douche. They are powerful drugs, and there is very little clinical evidence in favor of their employment at all.

W. A. *Bastedo.*

URESIN is a double citrate of lithium and urotropine, which, according to Kudintscheff and Soanki, has the power of diminishing the excretion of uric acid and of dissolving gravel. The dose is 1 gm. (gr. xv.).

W. A. *Bastedo.*

URETERS, PATHOLOGY OF.—Malformations of the Ureters.—The ureters take their embryonic origin from the lower part of the Wolffian duct. Malformations of the ureters are, on the whole, not very rare. If the kidney of one side is absent the ureter of the same side is generally absent also. Sometimes, however, in this case the ureter may exist, and then usually as a small duct. Absence of one kidney and ureter has been observed without any other malformation of the urogenital tract but kryptorchismus. Usually, however, in such cases other malformations are present, and uterus unicornis, absence of the vas deferens and a seminal vesicle, or a malformation of one side of the prostate, have been found.

Both kidneys and both ureters may be missing; in one case of this kind the fœtus lived ten minutes after birth. In cases in which the kidney was but incompletely developed, the ureter also showed incomplete development. In one such case the ureter did not reach the bladder; in another it had an abnormally small lumen.

A partial duplication of the ureter is not rare, especially in its upper part. Double ureters usually unite before they enter the bladder. A perfect duplication of the ureters is rare; in such cases the points of entrance into the bladder are generally near each other. They may, however, end as much as 1.5 cm. removed from each other. Double ureter is sometimes combined with a horseshoe kidney; in such a case three or even four ureters may apparently originate from one kidney. Sometimes two ureters end in two separate parts of one kidney on the same side. In this case the ventral ureter connects with the lower and ventral kidney, the dorsal ureter with the dorsal kidney, situated nearer the diaphragm. The first ureter enters the bladder at a higher level than the second ureter. This arrangement is similar to the one found in a doubling of the Wolffian duct. In the case of doubling of the ureter the pelvis of the kidney may also be double, or may be single; the latter occurrence is, however, much less frequent. Double ureters may be found on both sides or on one side only.

Of clinical importance are congenital valvular projections of the mucous membrane of the ureter, which are sometimes met with. These may be found in all parts of its course, especially, however, at the place of its entrance into the bladder and pelvis. If the concavity of such projections is directed toward the kidney they may obstruct the flow of urine and cause hydronephrosis. Such valves may become fixed by external adhesions. Congenital torsion of the ureter may have a similar significance.

Besides a valvular obstruction a congenital stenosis or atresia has been found, especially in the lower part of the ureter. It may be followed by a great dilatation of the upper part of the ureter and by a forward bulging of its lower part either outside or inside the bladder. In the latter case such a diverticulum may cover the internal meatus of the urethra. Such diverticula of the ureter have, however, also been found in cases in which the ureter was patent.

The ureters may enter the pelvis of the kidney in its centre instead of at its lowest point. Under these conditions the collection of urine in the lower part of the pelvis may entirely occlude the opening of the ureter. A similar result may be produced if the insertion of the ureter into the pelvis is an oblique one. A projecting part of the ureter may become pressed against the opposite side of the wall of the ureter by the collection of urine. Instead of running straight down to the bladder the ureter may be bent in its further course so that it forms an angle.

The ureter may enter the bladder higher up than is normal, or it may end in the urethra (colliculus seminalis), in the vesiculæ seminales (in the male), or below the external meatus of the urethra and in the uterus or vagina (female). A double ureter may have one normal and one abnormal ending.

Inflammation of the Ureters.—Inflammation of the ureters rarely starts in the ureters themselves. This may, however, be the case if a calculus becomes impacted in a ureter, or if during labor the ureters become compressed and injured. The mechanical lesion may be

[1] Annals of Surgery, April, 1903.

followed by a secondary infection with micro-organisms. Usually inflammation of the ureters is secondary to inflammatory changes in the kidney and pelvis of the kidney, to cystitis, or to inflammation of the ovaries or Fallopian tubes, or of the connective tissue included in the fold of the ligamentum latum. In the latter case the infection is carried to the ureters through the lymphatics; in the two former cases the propagation of the infection may take place either through the urine or through a continuous growth of the micro-organisms along the mucous membrane. On the whole, the ureters are not very favorable to inflammatory changes. Cystitis may exist for many years without the affection extending to the mucous membrane of the ureters. Inflammation may be found after a primary cystitis only in the pelvis of the kidney, the ureters remaining unaffected. These facts seem to indicate that the propagation of the infection from the bladder upward takes place principally through urine carrying micro-organisms and regurgitating into the ureters. Such a regurgitation can easily take place if, through an obstacle to the outflow of urine in the urethra for instance, first a dilatation of the ureters takes place. In this case the openings of the ureters into the bladder soon become enlarged as well. Experiments have shown, however, that even without a previous dilatation of the ureters, if the bladder is slowly distended through injection of a solution of methylene blue, the injected fluid in a certain number of cases may pass upward into the ureters.

Propagation of the inflammation of the kidney to the ureters may take place in cases in which the pelvis of the kidney is infected, as, for instance, in cases of stone in the pelvis or of pyelonephritis following abscesses in the kidney.

Anatomically, the mucous membrane is red (hyperæmia), œdematous, infiltrated by leucocytes, while its epithelial cells are thrown off in increased numbers. The infiltration with leucocytes may go so far that a purulent inflammation is produced. In severe cases in which decomposition of the stagnating urine takes place, we may find a diphtheritic inflammation of the mucosa. Dark membranes are formed, consisting of a fibrinous exudate and the necrotic superficial parts of the mucous membrane.

In severe chronic inflammations the mucous membrane may hypertrophy and form villous projections; in other cases a simple thickening takes place through proliferation of the connective tissue. The inflammation sometimes proceeds from the ureter to the connective tissue surrounding it, the latter becoming greatly thickened in consequence.

In certain cases of chronic inflammation (*ureteritis granulosa, nodularis, follicularis*) we find small gray miliary nodules in variable number disseminated in the mucous membrane of the ureters. They consist of collections of small round cells similar to or identical with the lymphocytes. It has been maintained that lymphoid tissue is normally present in the ureter and other mucous membranes. This is, however, not the case. In newborn children, and also in healthy adults, it may be entirely absent, although it may be found in cases in which no other sign of a past inflammation can be determined. If these nodules, however, are present in large numbers they probably point to a chronic inflammation. The mucous membrane around these grayish nodules is usually red and œdematous. These nodules have also been observed in typhoid fever and in diseases of the kidneys and of the heart. A similar anatomical sign of inflammation has been observed in the conjunctivæ.

Ureteritis Membranacea.—An inflammation has been described in which membranes, several centimetres long, are said to have been expelled from the ureters. So far a confirmation through post-mortem examination does not seem to have been recorded, this contention being based only on clinical evidence.

A condition without much clinical significance, yet of pathological interest, is the *ureteritis cystica*. In this condition the ureter is covered with superficial cysts. They are especially frequent in the upper half of the ureter, near the pelvis of the kidney; they are usually of the size of a pinhead and sometimes they are twice as large; they contain a material like mucus. Not rarely they are distributed in small groups in the mucous membrane, which may occasionally form polypoid processes containing these cysts. They are often found combined with inflammatory conditions of the ureters. They take their origin from the "Brunnschen Epithelnester," formed by an ingrowth of the ureteral epithelium into the connective tissue. These epithelial nests may branch and form secondary processes; at the surface they may become occluded by connective tissue, and the cells in their centre may become dissolved. In this way cysts are formed. The degenerating epithelial cells, together with certain products of the blood, may give rise to structures which probably incorrectly have been believed to be micro-organisms and the cause of the cyst formation. The structures, described by different authors as micro-organisms, are not identical, and they have also been interpreted in a different way by different investigators (myxosporidia, coccidia). Similar structures seem to be present in the colloidal cysts of the thyroid.

Tuberculosis of the Ureters.—A primary tuberculosis of the ureters is not known. Tuberculosis of the ureters is either descending, following tuberculosis of the kidney and of the pelvis of the kidney, or ascending, following tuberculosis of the bladder. How far the urine containing shreds of tuberculous material and bacilli is responsible for this propagation, and how far the bacilli spread by way of the lymphatics, has not been determined. That the urine is an actual source of infection is shown by the fact that in descending tuberculosis it is not uncommon for the narrowest part of the ureter near its entrance into the bladder to be affected, the upper parts remaining free. Involvement of the ureter in chronic tuberculosis of the kidney is frequent. The first tuberculous lesions of the ureters consist of small disseminated gray nodules of tuberculous tissue in the mucous membrane. They caseate and then form small ulcers. In the beginning the epithelium covering these nodules may have markedly proliferated, becoming horny, and forming cholesteatomatous plaques. In the mean time new nodules are formed near the first one, which also caseate and unite with the first. The outer part of the ureter and the surrounding tissue become thickened through proliferation of the connective tissue. The process progressing in this way, the ureter becomes often transformed into a tortuous tube, thicker than a finger, with cheesy masses inside and a thick fibrous wall. These cheesy masses may become incrusted with lime salts. The ureter frequently remains open, but it may become occluded by the cheesy masses or shreds of tuberculous tissue from the kidney. In ascending tuberculosis the same changes are first to be found in the lower half of the ureter.

Syphilis.—Lesions of the ureter, undoubtedly due to syphilis, have not been described. In certain cases of syphilis an inflammatory thickening of the wall of the ureter has been found. The syphilitic nature of this inflammatory change, however, is doubtful.

Foreign Bodies in the Ureters.—Stone in the ureter, in cases known so far, has been secondary to stone in the kidney or stone in the pelvis of the kidney. If small, such a stone may easily pass the ureter. If somewhat larger, it will be held back at the entrance of the ureter into the bladder. A large stone may obstruct the lumen of the ureter at any place, either permanently or for some time, until the force of the stream of urine presses it down into the bladder. In passing, a stone may injure the mucous membrane of the ureter and cause hemorrhage. If kept back at a certain place, hydronephrosis may follow. The outer wall of the ureter may become thickened through an inflammatory reaction, or the pressure of the stone may cause atrophy of the wall of the ureter, which can be followed by an actual rupture. In this way a stone may penetrate into the surrounding connective tissue, into the peritoneal cav-

ity, or into the intestines; or if the retention of the stone occurs at the lower end of the ureter, the stone may produce an artificial passage into the bladder.

The injury caused by a stone may be complicated by the settling of micro-organisms at such places; then pyelonephritis and pyonephrosis may follow, or near its wall at the place of injury an abscess, lodging the stone, may arise at the side of the ureter. If the ureter is entirely occluded by a stone, its lumen below the obstruction may become considerably shrunken.

In tropical and subtropical countries distomum hæmatobium and its eggs may live in the wall of the ureters, and may cause papillary outgrowths of the mucous membrane. Another parasite to be found, though rarely, in the ureters, is eustrongylus gigas. In cases of hemorrhages from the ureter or kidney, or of chyluria, coagula of blood or lymph may fill its lumen.

Obstruction of the Ureters.—The causes of obstruction to the flow of urine in the ureters may be the following: Calculus in the ureter, stricture in the ureter through inflammation of its mucous membrane, or through inflammation of the surrounding connective tissues. Compression of the ureter through exudates in the para- or perimetrium, or through enlarged lymph glands or a tumor. Obstruction caused by a projecting tumor, by tuberculous products, or by a coagulum of blood or lymph, by parasites, or by compression of the ureter through an abnormally situated branch of the renal artery. The formation of abnormal folds, or of a valve caused by the obliquity of the ureter's insertion into the renal pelvis, or a twist of the ureter on its long axis, may also obstruct the flow.

Inflammatory changes in the mucous membrane leading to a stricture may be caused by the injury of a calculus, or by an inflammation with formation of diphtheritic membranes. Stricture may follow an ascending inflammation, originally caused by the gonococcus; whether, however, the changes in the ureters are also caused by the gonococcus or are produced by a secondary infection with other organisms, is not certain.

Obstruction to the flow of the urine in the ureters may be caused by changes in the bladder or in the urethra. If the bladder cannot contract sufficiently, obstruction in the ureters may follow. The urine collecting behind the obstacle causes a dilatation of the ureters. The ureter may not only become dilated, but also tortuous. If the condition is a chronic one, the wall of the ureters becomes thickened; this thickening is produced by hypertrophy of the muscular coat. Inflammatory changes also are frequently present in the ureteral wall, contributing to the thickening. The result of a chronic obstruction is hydronephrosis and destruction of the kidney. If, as is often the case, micro-organisms are present at the point of lesion, or are added secondarily, a pyonephrosis follows. If an artificial stenosis of the ureter is produced in animals, hydronephrosis does not necessarily follow. Atrophy of the kidney may be the only result, and if a hydronephrosis does follow, the fluid may contain urine (uronephrosis).

In the case of a congenital obstruction to the flow of urine, hydronephrosis does not necessarily follow; simple atrophy of the kidney of the affected side may be the only result.

Tumors of the Ureters.—Primary tumors of the uterus, rectum, bladder, and kidney may secondarily affect the ureters. Carcinoma of the uterus frequently penetrates the wall of the ureters, causing hydronephrosis. In several cases one ureter was in its whole circumference included in a fibroma of the uterus, probably to be explained by secondary concrescence of originally separated fibromatous nodules.

Primary tumors of the ureters and the pelvis of the kidney are rare. Benign papillary tumors and carcinoma have been found most frequently; myoma striocellulare, sarcoma, and endothelioma are very rare. The ordinary papilliomata consist of a fibrous centre covered by one or two rows of epithelial cells. Tumors showing a transition from typical benign papillomata to carcinomata of a papillomatous structure have been found. Typical papillomatous carcinomata also have been described; these are rarer than the benign papillomata.

The fact is of importance that in several well-authenticated cases the epithelium of a papilloma which had existed for some time as a benign tumor, later on began to infiltrate the deeper tissues, thus becoming a carcinoma. Besides the papillomatous variety of carcinoma, the ordinary non-papillomatous carcinoma has been found in the ureters and in the pelvis of the kidney. It may have the character of an alveolar carcinoma with cuboidal cells, or it may be of the cylindrical-celled or of the squamous-celled variety. Transformations of the epithelium of the ureter into the stratified squamous type have also been observed without the presence of a tumor (leucoplasia).

It is of interest to note that quite a number of benign papillomata, or indeed of carcinomata, may be present at the same time, and that tumor nodules may even extend the entire length of the ureter, reaching the bladder. The favorite sites for the isolated as well as for the multiple tumors are the pelvis of the kidney and the vesicular end of the ureters. This suggests a certain analogy to the favorite seat of œsophageal neoplasms.

The multiplicity of malignant tumors may be caused by implantation of cells carried away by the urine and kept back at places where a greater resistance to their passage is offered, or to metastatic growth along the lymph channels. Whether the multiple occurrence of the benign papillomata is to be explained in a similar way, is still doubtful. In several instances the origin of the neoplasms has been connected with the presence of a stone in the ureter. No convincing case, however, has been reported so far. A problem is thus presented similar to that in connection with the gall bladder.

The tumors of the ureters may cause hydro-, hæmato-, and pyonephrosis. Carcinoma of the ureters may spread to the kidney, bladder, seminal vesicles, lymph glands, and peritoneum, and may cause metastases in the liver pleural cavity, and lung. *Leo Loeb.*

URETERS, SURGERY OF THE.—The ureter is a flattened, whitish tube which connects the pelvis of the kidney with the bladder. It begins at the level of the twelfth rib, about 4 cm. (1.6 in.) from the median line. It crosses the pelvic brim one-third of the distance, that is, about 3 cm. (1.2 in.) from the median line, to the anterior superior iliac spine. It can be palpated just above the brim of the pelvis. In the pelvis it lies just in front of the common iliac artery and then curves sharply forward to pierce the base of the bladder (Fig. 4839). In the abdomen it lies upon the psoas magnus muscle. Either the right or the left ureter can be exposed without opening the peritoneum, through an oblique incision parallel with and a little above Poupart's ligament. The ascending or descending colon is freed and pushed toward the median line, exposing the ureter.

The length of the ureter is from 25 to 30 cm. (10 to 12 in.). The function of the ureter is simply to transmit urine which collects in the pelvis of the kidney. This is done by a slow peristaltic action. The portion of the ureter close to the bladder can be palpated in man through the rectum, while in woman the lower end of the ureter can be palpated to a distance of 5–8 cm. (2–3 in.) through the vagina. If there is a stone in any portion of the ureter the lower end is said to be extremely sensitive.

Traumatisms.—Injury to the ureter is not common. It may be opened by stab or gunshot wounds, or torn by the passage of a wheel across the abdomen. If it is torn clear across, little or no blood will enter the bladder, so that the urine passed from the bladder may be entirely clear. If it is partially torn, some urine from the injured side may reach the bladder. In either case there will be a retroperitoneal extravasation of urine, with more or less obstruction in the corresponding kidney. Such a condition was formerly treated by repeated aspirations. At the present time the proper procedure is to expose the

ureter, to suture or tampon the wound, or to resect and suture the ureter if the injury is more severe. In any case drainage should be employed. If the ureter is injured beyond hope of repair, or if there is reflex anuria threatening the life of the patient, nephrectomy should be performed.

The ureter is frequently injured in pelvic operations, being cut or seized in a clamp or ligature. This is especially the case in operations for carcinoma of the uterus, while the tube is less often injured in operations for carcinoma of the rectum, because the regional lymph glands in the latter disease are not so near the ureters. The patient may die from ureteral infection, or from obstruction to the urinary flow, or he may recover with a urinary fistula. Long-continued pressure during childbirth may cause necrosis of the wall of the ureter and a fistulous communication between it and the uterus or vagina. Many plastic operations have been devised for curing such a fistula. They consist either in the re-establishment of the wall of the ureter, or in its implantation into the bladder higher up. Details of this operation are given in text-books on gynecology. Many operators make it a practice at the close of a difficult pelvic operation to examine the ureters so as to make sure they have not been injured. It is also a good practice in many cases to insert a ureteral probe before operation to serve as a guide to prevent injury of the ureter.

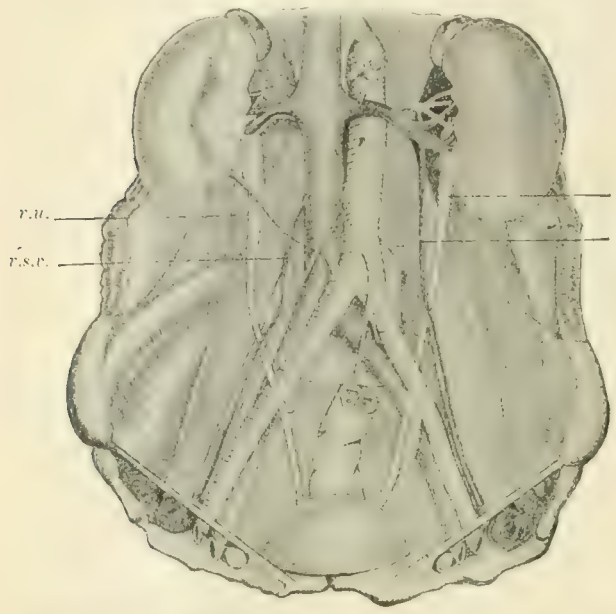


FIG. 4839. Relations of Ureters. *r.u.*, Right ureter; *l.u.*, left ureter; *r.s.v.*, right spermatic vein; *l.s.v.*, left spermatic vein.

Inflammations.—Ureteritis rarely occurs as an independent disease; it forms a part of the general inflammation of the urinary tract. Gonorrhœal inflammation of the ureter may give rise to the formation of ureteral valves and strictures. Tuberculosis changes the whole ureter into a stiff, inelastic tube. In acute inflammation the ureter is very tender, and in chronic inflammation it is thickened. Both of these conditions may be recognized by abdominal palpation in not too stout patients, and also by examination through the rectum or the vagina. Any obstruction in the ureter is of the greatest importance, since it may lead to hydro- or pyonephrosis.

There is a disease known as chronic polypoid ureteritis, in which the mucous membrane of the ureter is thickly studded with cysts.

If a renal calculus becomes blocked in its passage through the ureter a suppurative periureteritis may be produced. The pus which forms around the ureter will soon destroy its wall, giving rise to extravasation of urine.

Obstruction.—The lumen of the ureter may be blocked by a foreign body, such as a calculus, or a blood clot, or an existing inflammation, or the effects of a previous one, or by pressure of a tumor or a focus of inflammation outside of the ureter. The best treatment is of course to remove the cause if possible.

TREATMENT.—An inflammatory condition may be treated by irrigation. Strictures of the lower end of the ureter may be dilated by metal catheters, varying in diameter from 2 to 5 mm. (0.1 to 0.2 in.).

If a ureter is ruptured by traumatism or accidentally cut across during an operation and its ends are freshened and sutured, the continuity of its lumen will in most cases be restored. If the condition is such that owing to damage of a portion of the ureter or a stricture a resection is necessary, suture at once becomes more difficult. Schopf first sutured the ureter in 1886, inserting stitches which did not puncture the mucous membrane. Bovée suggested the idea of cutting the ends of the ureter obliquely so that the resulting scar should not be a circular one. D'Antoma invaginated the central end of the ureter into the peripheral one, which he split up to facilitate the operation, and then closed by suture. Van Hook inserted the central end into a lateral split in the peripheral end (Fig. 4840). The peripheral end is ligated above the lateral slit. All of the methods of suture described have been successfully employed. The methods of implantation, as shown by experiments upon animals, give the greatest safety against leakage. Unfortunately these methods may be impracticable on account of the loss of a portion of the ureter. This tube has a certain elasticity, so that direct suture may be possible, even when the loss amounts to as much as 8 cm. (3.2 in.). The nutrition of the ureter is kept up by two small arteries which spring from the renal artery and accompany the ureter almost to the bladder; hence in isolating the ureter for the purpose of suture, it should not be peeled bare of its surrounding connective tissue. When the operation is finished, the ureter should be covered with peritoneum or other living tissue and not surrounded with gauze.

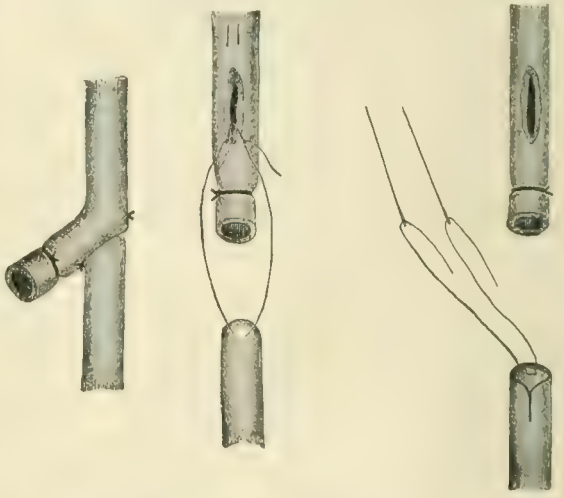


FIG. 4840 Illustrates Different Methods of Reuniting the Cut Ends of the Ureter after a Portion of the Tube has been Resected. (Van Hook's lateral uretero-ureteral anastomosis.)

If the defect in the ureter is situated at its upper end,

it may be possible to suture the peripheral portion of the ureter into the pelvis of the kidney. If the defect is in the lower portion of the ureter, the central end may be implanted in the upper part of the bladder. Such an implantation, if possible, should be made extraperitoneally. In some cases the sutures employed have been drawn out through the urethra. Witzel and others have implanted the ureter obliquely in the vesical wall so as to prevent the back flow of urine. In most of these cases a catheter has been left in the bladder for a few days.

The ureters have several times been implanted in the rectum or sigmoid flexure, but the success of this operation is a limited one, as most of the patients have died from peritonitis or pyelonephritis or hydronephrosis.

Edward Milton Foote.

URETHANE.—By the simple title *urethane* is understood, in medicine, the body *ethylic urethane* (ethylic carbamate) $NH_2.COOC_2H_5$. This compound occurs in colorless tabular crystals, soluble in water, alcohol, and ether. It has no odor and but a mild ethereal taste, producing a sensation of coolness in the tongue. Urethane operates upon the animal system as a quite pure, though not overpowerful hypnotic, without effect upon the peripheral sensory apparatus, and without untoward effects of any kind. It is used in medicine for procuring sleep, and is found fairly efficient in the more tractable conditions of insomnia. Doses of 1 gm. (gr. xv.) commonly suffice, but the drug may be required in two or three times this quantity, and such large doses have been perfectly well borne. The remedy has also been administered by hypodermatic injection. From the uncertainty of its operation, urethane has not established itself as a valuable medicine and is not official in the United States Pharmacopœia. It may be prescribed in simple aqueous solution.

Edward Curtis.

URETHRA, INJURIES AND DISEASES OF THE.—Anatomy.—The urethra under normal conditions is a closed canal, averaging about eight inches in length. It is to be divided, both anatomically and clinically, into two chief parts, the anterior and the posterior urethra.

The anterior urethra is that portion which extends from the meatus to the anterior layer of the triangular ligament. This portion is on the average about six inches in length, and is itself divided into three portions, which have somewhat different clinical characteristics. The first portion extends from the meatus backward for about one-half an inch. It is somewhat wider in its central portion than at either of its extremities, and is therefore known as the fossa navicularis. The constriction at its posterior extremity is occasionally of some importance, as the point of an instrument may become arrested and its further advance prevented until a proper direction is given.

The next, or median portion, extends from the fossa navicularis backward for about three and one-half inches. It is without constriction, and may be regarded as representing the calibre of the urethra, and should in health permit the introduction of a No. 26 F. sound without stretching.

The portion of the urethra lying behind this median portion and in front of the triangular ligament is known as the bulbus urethræ, or bulb. It is a more distensible and roomy portion of the urethra, and under pathological conditions or in old people may be dilated so that a pocket occurs just in front of the triangular ligament. This portion of the urethra is important because, owing to its distensibility, the floor is here readily pushed downward by an instrument advancing along the urethra until it lies below the level of the opening in the triangular ligament, and the instrument is then arrested because its point comes sharply against the ligament, and false passages are here of common occurrence. It is also to be remembered that in inflammatory conditions of the urethra the disease is apt to remain longer in this region, possibly owing to the fact that it is the most dependent portion of the fixed urethra and infectious materials gravitate into it.

The deep urethra, or that lying between the anterior layer of the triangular ligament and the urethral orifice of the bladder, is from one and three-quarters to two inches in length on the average. It is divided into two portions: that lying between the anterior and posterior layers of the triangular ligament, or the membranous portion, and that lying behind the posterior layer of the triangular ligament and surrounded by the prostate or the prostatic urethra. The membranous portion, as its name betokens, is easily distensible, and prone to injury both from instruments and from external violence.

The prostatic urethra, or that portion lying within the prostate, is interesting chiefly as containing the orifices of the ejaculatory ducts and of the glands of the prostate. It is divided at the centre of the floor by a median elevation known as the verumontanum. This contains a furrow in its anterior portion into which open the ejaculatory ducts, and it is known as the sinus pocularis. It is believed to be the homologue of the uterine cavity in the female. On either side of the verumontanum lie the prostatic sinuses, so called, into which open the ducts of the prostatic follicles.

While the anterior urethra may be artificially considered as a straight canal, it is not so under normal conditions. The posterior, or bulbous portion, is more or less fixed in the perineal tissues, having in the erect position an almost antero-posterior direction, though rising somewhat in its anterior portion. With this the penile portion makes a sharp angle, owing to the pendulous position of the anterior urethra, and the angle so formed is commonly known as a penoscrotal angle. It is important as being commonly the seat of sensitive granulations following inflammatory diseases of the urethra, and of so-called spasmodic stricture and strictures of large calibre.

Glands of the Urethra.—The anterior urethra is plentifully provided with small glands situated in the submucous layer and opening into the urethra by ducts running forward. These are known as the glands of Littré, and are of prime importance in inflammatory conditions of the urethra.

Cowper's glands lie between the layers of the triangular ligament on either side of the membranous urethra, and open by ducts of considerable length into the bulbous portion of the urethra.

The prostatic follicles or glands, above referred to, lie among the muscular fibres of the prostate gland.

INJURIES OF THE URETHRA.

The pendulous portion of the urethra is, owing to its great mobility, little liable to injury, though it may, of course, be injured by cuts, stabs, or crushing accidents involving the whole pubic region.

The bulbous urethra is the most liable to accident, and next to that the membranous urethra.

Rupture of the Urethra.—*Etiology.*—Injury to the urethra occurs most frequently by falls upon the perineum astride some hard object, as a beam, fence, or chair. Under these circumstances the urethra is forced against the pubic ramus upon either side, the force of the blow rarely being exactly median. The injuries taking place in this way may vary from very slight and trifling lacerations to complete transverse division of the urethra.

It may be mentioned here that another not uncommon form of injury to the urethra is from the careless use of stiff instruments, which tend to leave the urethra in the region of the bulb, especially where inflammatory processes have damaged the mucous membrane. The injury in these cases may vary from slight punctured wounds to complete transverse division, as in one case, seen by the writer, in which violent efforts to pass a silver catheter upon an old man with prostatic obstruction resulted in rupture of the bulbous urethra, with the formation of a large blood clot closely simulating conditions found in traumatic rupture of the urethra. It may in general be said that the amount of injury, particularly that due to

violence, is greater than either the signs or symptoms would indicate, and for this reason a false sense of security may lead to the neglect of patients, with considerable damage to the bulbous or membranous urethra.

Pathology (*Clinical*).—When any considerable rent has occurred in the urethra, the train of symptoms following is due to the extremely irritating qualities of the urine which infiltrates the tissues. The rapidity with which spreading gangrene may take place from infiltrations of this character is hardly equalled by any process seen elsewhere in the body. The direction in which the infiltration will spread depends upon the anatomical arrangement of the fasciæ in this region, and is so characteristic as to require careful consideration. When rupture takes place in the bulbous portion of the urethra, infection will spread to the tissues of the scrotum and then upward through the space between the pubic spine and the insertion of the fascia into the symphysis. It will not tend to go downward on to the thigh, owing to the adhesion of the superficial fascia in the region of Poupart's ligament. Having once gained access to the front of the abdomen through the space above mentioned, it may spread upward to almost any extent. In the later stages the spread may be more atypical, owing to the breaking down of the natural barriers. If the rupture take place in the membranous portion the extravasation will follow the layers of the pelvic fascia, spreading between the fascia and the wall of the pelvis, and possibly reaching the thigh through the space on the inner side of the femoral vessels. If rupture occur in the prostatic urethra the infection will extend into the connective tissue in the pelvis between the fascia and the peritoneum, and pelvic abscess may result. Rupture of the prostatic urethra, except when due to instruments or sharp spicules of bone, in fracture of the pelvis, is almost unknown.

The most characteristic pathological phenomenon of traumatic rupture of the urethra is the formation of a blood clot. This will generally be found in the perineal region between the scrotum and the anus, and will vary from a very small quantity to an amount sufficient to cause a bulging tumor as large as an orange. At first this blood is unmixed with urine, but as the bladder becomes distended leakage will take place, and the size of the tumor may be considerably increased by additions from this source.

Rupture occurs most commonly upon the floor of the urethra, and in the more extensive cases the urethra may be completely divided, with the exception of a small strip of mucous membrane on the upper wall.

The elasticity of the tissues forming the urethra is great, and the tendency of the ends to retract is marked, but not excessive except where complete division of the urethra has occurred, when the retraction may separate the divided ends of the urethra for a considerable distance, the intervening space being filled with blood, urine, and tissue detritus.

Symptoms.—Pain is not a characteristic symptom of rupture of the urethra, and extensive damage may exist without causing severe pain except on micturition. The contact of urine with the raw surfaces is always extremely painful, but with this exception pain may be striking by its absence.

Hemorrhage.—A small amount of bleeding from the meatus is quite characteristic of damage to the urethra. This is usually seen in the form of a few drops of blood, which appear shortly after the injury, and a little intermittent oozing is likely to continue for some time if treatment is not instituted. Hemorrhages of considerable amount are extremely rare, though instances have been occasionally reported.

Retention of Urine.—This symptom is quite characteristic of rupture of the urethra. Generally the patient will be unable to empty his bladder at all, though in the milder degrees the attempt may be successful at first, and later fail on account of swelling which occurs about the injured part. This symptom, taken in connection with the slight bleeding from the meatus and the history of injury, is almost pathognomonic of rupture of the urethra.

Tenesmus.—Where the damage is sufficient to cause retention, tenesmus will always follow after a longer or shorter time. As the bladder distends, leakage takes place into the injured area, and the pain results in violent bladder tenesmus, which is likely to cause an increase of the bleeding from the meatus. This symptom, while constant, is not of great importance, as it will occur only in the presence of other symptoms sufficient in themselves to warrant the diagnosis.

Shock.—In rupture of the urethra uncomplicated by fracture of the pelvis or extensive damage to other tissues, shock is not a prominent symptom, though it may readily occur when the blow causing damage to the urethra has at the same time struck one or the other testicle with sufficient violence to cause the rather characteristic symptoms of shock from this cause. When rupture of the urethra is a complication of extensive crushing injuries involving the pelvis, shock may be a prominent symptom; but in these cases it is a symptom of injury to other tissues rather than to the urethra.

Fever.—The occurrence of fever after rupture of the urethra is not an immediate symptom. It comes only when infection of the blood clot has taken place, and is, therefore, too late a symptom to be of diagnostic value.

Treatment.—When, from the occurrence of any of the above symptoms, rupture of the urethra is suspected, an attempt should be made to enter the bladder with a soft instrument. This may occasionally be successful, but will on the whole do more to confirm the diagnosis than to prove itself of value in the treatment. The instrument will generally leave the urethra at the point of rupture and impinge upon some of the irregularities which the injury has caused. If a stiffer instrument is to be tried, the attempt must be made with the greatest care, the attendant bearing in mind the fact that he will probably fail, and that it is his duty to do no further injury to an already damaged urethra. In general it may be said that, should a soft instrument fail to find its way into the bladder, no further instrumentation should be undertaken until all preparations have been made for any operation which may be necessary to insure success, for to attempt to enter the urethra with a stiff instrument without being prepared to take the consequences should failure result, and resort immediately to a cutting operation, is little short of meddlesome surgery.

If the means for radical operation be not at hand, overdistention of the bladder may be prevented by aspiration above the pubes. This is not to be regarded as a curative measure, and will not prevent the leakage of urine into the damaged tissues, but it may contribute to the comfort of the patient during necessary delay.

The operation of election is perineal section, with evacuation of the blood clot, and if possible union of the divided ends of the urethra. There is a growing tendency among surgeons to do this operation, even in cases in which, under ether, an instrument can be made to pass. This comes from the conviction that the amount of scar tissue following the injury will be less when treated by the open method, and from the very general experience of the intractability of urethral strictures resulting from this accident.

The first step in the operation should be the attempt to pass a full-sized sound. This will probably fail, but in case of success it may be used as a guide to perineal section. If it fails it may still be used as a guide to the point of rupture. The patient should then be placed in the lithotomy position, and a median incision made in the perineum. When the blood clot has been evacuated and the bleeding, which is generally most marked from the posterior end, controlled, search should be made for the ends of the urethra. The anterior end can generally be found without difficulty, as the instrument in the urethra is a direct guide to its position; but the discovery of the posterior portion may be a matter of difficulty, or even impossibility.

We cannot here go at length into the methods of search. If, after a considerable search, the posterior fragment cannot be found, recourse should be had to retrograde

catheterization. For this purpose the bladder is opened above the pubes, as described in the section on suprapubic cystotomy. The catheter is then passed from the bladder into the wound, and the posterior fragment of the urethra can generally be located. This having been done, the further procedure is the same in either event.

It is generally thought wise to attempt to unite the divided ends of the urethra and thereby diminish the amount of scar tissue. This is best done with catgut sutures, which may or may not include the mucous membrane. When the wound has been largely closed two courses are at our disposal: either a large soft-rubber catheter may be passed into the bladder and tied in place, or it may be passed down to the point of rupture and the bladder drained with a perineal tube. In either case no further closure of the wound with sutures is indicated, and a light packing of gauze should be left in position. The rest of the treatment is so similar to that after perineal section for stricture that its further discussion will be unnecessary here.

Rupture of the pendulous portion of the urethra will be accompanied by extravasation into the tissues of the penis, with rapid swelling, œdema, and tissue necrosis, unless relieved. Incision should be prompt and free, the wound in the urethra sutured or not, according to its extent, the external wound packed with gauze and the bladder drained with a catheter.

Foreign Bodies in the Urethra.—Foreign bodies in the urethra are of two classes: those introduced from without, either by the patient or by the doctor, and those coming down from above, as, for instance, stones which, having passed the ureter, have become impacted in the urethra and obstruct the passage of urine.

Of the foreign bodies introduced from without there are an immense variety, of which detailed account cannot be given here, and their introduction by the patient is generally due to some mental perversion. Occasionally pieces of instruments or catheters may break off and be left in the urethra. In these cases their presence is at once known and the proper measures can be taken.

Foreign bodies left in the anterior urethra can occasionally be forced out by pressure on the urethra, but such an occurrence is unusual. They may frequently be removed by the introduction of a full-sized endoscope in a good light, the body being seized with proper alligator forceps. In order to prevent it from slipping back along the urethra, which it has a marked tendency to do, the fingers of the left hand should compress the urethra behind it and prevent such slipping. In case removal by the endoscope is impossible, an external urethrotomy over the body is always proper, and the only necessary precaution is to make sure that the body is firmly held in position before the incision is made.

Foreign bodies in the deep urethra can rarely be reached by means of the endoscope. By far the most common of these bodies are urethral calculi which are too large to pass the urethra. In these cases they cannot infrequently be pushed back into the bladder by the use of a full-sized sound, and where this can be done without undue violence it will serve to relieve the retention which always exists. Once they have been pushed back into the bladder, they may be removed by the measures appropriate to stone in the bladder. When, in rare instances, they cannot be pushed back as above described, a small perineal incision or boutonnière can be made, and, with the forefinger of the left hand in the rectum, the foreign body can be grasped with dressing forceps and removed.

INFLAMMATORY DISEASES OF THE URETHRA.

Inflammatory conditions affecting the urethra may be classified under four general headings. These are: 1. Gonorrhœal. 2. Simple. 3. Syphilitic. 4. Chancroidal.

Gonorrhœal Inflammation.—The space at our command will not permit us to digress into the interesting discussion of the relation of the gonococcus of Neisser to this disease. Suffice it to say that gonorrhœal processes are always due to the above-mentioned organism, and that when doubt of its presence exists the classification cannot be made with certainty. The occurrence of other organisms closely resembling the gonococcus in staining properties and morphological characteristics is now beyond question, and in doubtful cases the question can only be decided by cultures.

Pathology.—The prime characteristic of this organism, as revealed in the varying severity of the inflammations which it causes, is its affinity for mucous membranes. While the gonococci are capable of producing inflammatory processes elsewhere, these inflammations are atypical and do not show the same virulent characteristics as are observed in the urethra. Another extremely important characteristic is the liking of the gonococcus for the deeper layers of the mucous membrane and for the glandular structures lying in the submucous layer. Upon this characteristic depends the extremely unsatisfactory results of treatment, as the gonococcus, once fairly established in the deeper layers, can be reached with difficulty, if at all, and may slumber for months, or even years, in some of these obscure hiding places.

Symptoms.—Acute infection. Where an acute, fresh infection or original infection has occurred, a well-marked period of incubation will always be found, and the absence of such a period should give rise to serious doubt as to the diagnosis. Infections with other organisms of a transient, unimportant character, and so-called "flare-ups" of previous infections, will show little or no period of incubation, but a fresh infection, uninfluenced by previous conditions, will always show a well-marked period of incubation, varying from four to seven days.

The first symptom is as a rule a slight itching or smarting of the urethra accompanied by a moderate mucoid discharge. In ordinary cases this rapidly increases during the following day or two, and the patient has severe burning on urination with a profuse yellow or greenish purulent discharge. In many cases about this time a certain amount of swelling and œdema appears. This is first noticeable around the meatus, and is evidenced by a slight pouting of the urethra. This is followed by œdema of the penis—sometimes extreme,—probably due to lymphatic obstruction. The lymphatics, especially upon the dorsum, are often to be seen as well-defined red marks, extending up to the region of the pubes. The glands in the groin at this time are frequently somewhat enlarged and tender. As a rule they do not go on to suppuration, and are in this way to be distinguished from the suppurating glands most commonly seen with chancroidal ulcerations. They are generally more marked upon one side than upon the other, and subside without local treatment.

In the absence of treatment the discharge and inflammatory symptoms continue to increase for from ten days to two weeks. The subsidence without treatment is a slow process, and probably in uncomplicated cases lasts for from six to eight weeks, at which time a certain proportion of untreated cases may be spontaneously cured.

The occurrence of any complications, however, may immensely protract the course of the disease, and there are some cases which have earned for themselves with some justice the title of "incurable."

Posterior Infections.—The disease starts in the anterior urethra, generally in the region of the fossa navicularis, and tends to extend slowly backward by continuity. In many cases it ultimately involves the greater part of the anterior urethra. In a considerable proportion of cases there is extension to the posterior urethra. This extension is frequently due to continuity of the process, but may undoubtedly be favored by the incautious use of instruments, or by injections, and has long been held up as an argument against the use of local treatment during the acute stages. Infection of the posterior urethra opens the way to a great variety of complications which do not belong strictly to the urethra itself; that is to say, prostatitis, seminal vesiculitis, epididymitis, orchitis, and Cowperitis. These do not fall within the scope of this article, and for their discussion the reader is referred to the sections on these conditions.

The distinction between a posterior urethritis and a prostatitis is hardly to be made, and it is probable that comparatively few cases of posterior infection occur without some involvement of the prostate. The symptoms of a posterior infection are quite different from those of an uncomplicated anterior urethritis, and it is frequently possible to decide that the infection has passed the triangular ligament. Thus, frequency of micturition is an almost unfailing symptom, and may vary from a very moderate increase to an almost persistent tenesmus. Pain is likely to be a prominent symptom, and the amount of pus coming with the latter portion of the urine will be found to be increased. Not infrequently the amount of discharge from the anterior urethra decreases at this time, and this has been held as an almost pathognomonic sign of posterior infection; but while it very generally occurs, it cannot be regarded as distinctive, and the reasons for its occurrence have not been satisfactorily explained.

Treatment of Acute Anterior Urethritis.—For many years the effort has been made by surgeons to abort this disease, and from our knowledge of the infectious agent this is theoretically possible. Practically, however, we rarely see these cases at a sufficiently early date, as symptoms sufficient to attract the patient's notice do not as a rule occur until the micro-organism has reached the deeper layers of the mucous membrane and has become relatively inaccessible. Where we have an opportunity to treat a patient, known to have been exposed, before the occurrence of symptoms, we are rarely in a position to postulate that infection would certainly have taken place, and claims of this kind are not therefore entitled to weight. Nevertheless, certain cases may be, if not actually aborted, at least cut short, and it is entirely permissible to attempt to abort cases seen within twenty-four hours of the appearance of symptoms.

The methods most generally employed are the use of antiseptic injections, or irrigations of the anterior urethra, considerably stronger than would properly be used in more developed cases or for any considerable length of time. Solutions of nitrate of silver (one to three or four grains to the ounce), of argonin and protargol (from two to five per cent.), and argyrol (from five to ten per cent.) are among the best. In order to be successful the treatment must be carried out mostly by the surgeon himself.

A fair sample of these methods is the following: A patient seen with a moderate muco-purulent discharge containing gonococci is given an injection in the anterior urethra of a solution of nitrate of silver, two grains to the ounce. This will produce a considerable burning, which will subside in from one-half to two hours. If seen in the morning the patient may be instructed to return later in the day, when an injection of the same solution, about one-half strength, may be given. He may then be given a solution of one of the silver salts of comparatively mild strength—as, for instance, a one-per-cent. solution of protargol—and told to use it himself as an interior injection, twice before the next visit on the following morning. A stronger solution of one of the silver salts, as, for instance, a three-per-cent. solution of protargol, may then be given by the surgeon, while the patient uses his own solution at noon and the stronger injection is given again at night. In the more favorable cases the discharge may be promptly checked and the gonococci will rapidly disappear, and by the end of a week the case may be in the subacute stage and run a comparatively short course.

Most cases, however, will not be proper subjects for this abortive treatment. Treatment is both general and local, and the opinion is gaining ground that both forms of treatment are of value for patients who really want to get well. This remark may seem unnecessary, but there are a considerable number of patients, more especially those seen in hospital practice, who will not give sufficiently regular attention to their disease to make its elaborate treatment worth while. These patients are, therefore, best given general treatment and not subjected to local measures until the acute stage has so far subsided as to make treatment at very short intervals unnecessary.

General Treatment.—This includes hygienic measures and diet. It is important to advise scrupulous regard for the general health and avoidance of dissipation or excess in any direction. Alcohol must be absolutely interdicted, and we have frequently seen ginger ale do harm. Highly seasoned irritating foods, fatty, fried, or strongly acid foods are also objectionable. Smoking, except to excess, is not objectionable. The drinking of large quantities of liquids—water, or perhaps better, milk—is valuable as a diuretic, and in this connection the use of alkaline diuretics, as the acetate or citrate of potash, is useful. Careful instructions in regard to the infectious nature of the discharge and the importance of personal cleanliness should never be omitted.

Of the drugs known to have a beneficial effect upon the mucous membranes of the urinary tract the following are the chief: balsam of copaiba, oleoresin of cubebs, sandal-wood oil, salol, and urotropin.

The balsams undoubtedly have some effect upon the mucous membranes to which they are conveyed by their solution in the urine.

Copaiba is perhaps best suited to the poorer class of patients, to whom expense is important. It is likely to disagree with the stomach and not infrequently produces erythematous rashes, which promptly disappear upon withdrawal of the drug.

Cubebs is much in the same class with copaiba. It is slightly less nauseating, and in our experience somewhat less efficient.

Sandal-wood oil is the most effective, but most expensive of this group. In order to act properly it must be pure, and on account of its expense it is frequently adulterated. When given in capsules it does not often upset the stomach, and its most common unpleasant effect is pain in the lumbar region. This may be combated by the use of moderate doses of salol, but in some cases it will force the abandonment of the drug.

Salol is regarded as a urinary antiseptic, and is excreted in the urine as salicylic acid and carbolic acid. Urotropin comes much under the same heading, and acts by virtue of the formalin which it liberates. We have personally not seen good results from the use of these drugs in acute urethritis, and do not regard them as likely to appeal to the mucous membranes in the same manner as do the balsams.

Patients who cannot or will not come frequently to see the surgeon may be treated as above described, with advice and balsams, and they will probably get well somewhat more quickly than if left untreated.

Local Treatment.—This consists in the application of antiseptic and astringent solutions to the anterior urethra. It may be done by injection or by irrigation. Injections are given with a small blunt-pointed syringe, holding from one to two drachms, by means of which the anterior urethra is distended without the use of force sufficient to drive the solution into the posterior urethra. Irrigations are carried out with a soft-rubber catheter (which is advanced slowly along the urethra, washing it out continually as the catheter advances) or with a blunt nozzle, through which a considerable stream is injected into the urethra, at first with sufficient force to close the cut-off muscle. After the anterior urethra has thus been irrigated the solution may be allowed to flow back into the bladder, and is then passed, thus thoroughly washing both the anterior and the posterior urethra (Fig. 4841).

The distinctive characteristics of these two methods are that the method of injection uses small quantities and depends upon antiseptic and penetrating properties, while the method of irrigation uses solutions less active and depends upon the quantity used, in part at least, for its mechanical effect.

The solutions used for injection are chiefly the silver salts. These, with the exception of nitrate of silver, are all comparatively modern products and are to some extent still in the experimental stage. Their claims to use-

fulness depend upon the fact that they are organic salts of silver and are not precipitated, as are the inorganic. They thus have greater power to penetrate to the deeper layers of the mucous membrane, and theoretically, at least, are more likely to reach the organisms beneath. There are several of them at present which have each their ardent advocates, and we cannot undertake to discuss their relative efficiency. Argonin and protargol may be used in strengths varying from one-half to four per cent. The citrate of silver should be used saturated, which is about one to four thousand, and the newest candidate for favor, argyrol, may be used in from one to ten-per-cent. solutions. They are all less irritating than the nitrate of silver, and the evidence goes to show that their claims to attention are substantial.

Where injections are to be used they should be given at least once a day by the surgeon himself, and during the acute stage the patient should use a less powerful solution twice or three times more in the twenty-four hours. The number of injections may be decreased as the inflammation subsides. All solutions used in this way should be held in the urethra for from five to ten minutes, as in this way their efficiency is much increased.

The solutions most commonly used for irrigation are permanganate of potassium of strengths of from 1 to 3,000, to 1 to 6,000; corrosive sublimate, 1 to 10,000 to 1 to 50,000; and nitrate of silver, 1 to 4,000 to 1 to 8,000. Irrigation should always be carried out by the surgeon himself, and there can be no doubt that when carelessly used it is capable of doing great harm. We do not believe that it is a procedure which can safely be left to the patient, and think that its greatest field of usefulness is in connection with injections, the irrigation being given by the surgeon and the injection used by the patient. Since these irrigations depend for their efficiency in part upon the quantity used, this should always be considerable, and most authorities agree in advising the use of from one to three pints. If the solution prove irritating to the anterior urethra it should be diluted before it is allowed to flow back into the bladder. The method in which a catheter is employed and the urethra cautiously irrigated inch by inch, from the meatus to the bulb, care being taken to see that a free back flow is kept up, commends itself to us as being less liable to be followed by complications, and we are inclined to think that for practitioners who are not specialists this method is likely to be most generally useful.

Treatment of Acute Posterior Urethritis.—The occurrence of this form of inflammation has already been noted. When this is confined to the urethra itself the process may occasionally be headed off by the use of instillations of nitrate-of-silver (from one to five grains to the ounce), of which solution five to ten drops should be used. As a rule, however, these cases do best when not treated locally during the acute stage. For a further discussion of this the reader is referred to the pages in the article on *Prostate, The,* in Vol. VI.

Chronic Urethritis.—This name is given to the cases which, with or without treatment, continue for an undue length of time. As a rule the only symptom is a very moderate discharge, most noticeable in the morning, and the more or less constant presence of shreds in the urine. It generally is not a source of annoyance to the patient, except from the knowledge that he is not cured. It is far more to be dreaded as a source of infection than the more acute conditions, as the very mild symptoms lull the patient to a false sense of security or are overlooked through ignorance of the damage which they may cause. The treatment belongs really in the province of the specialist, and obstinate cases are likely to be a source of considerable annoyance to the general practitioner.

Continuance of the inflammation is frequently due to infection of the prostate or seminal vesicles, or to a stricture, and for a discussion of these causes the reader is referred to other sections of the present article. Another not uncommon cause is the so-called granular patches, or granulations, in the urethra. These are small areas, most commonly found in the bulb or at the peno-scrotal angle, where the infection has persisted in the deeper layers with more or less destruction of mucous membrane. These patches can best be treated with the endoscope. An instrument should be selected as large as the urethra will accommodate without causing undue pain. This should be passed to the region of the bulb and the obturator withdrawn. Then, with a good illumination, the surgeon should follow the whole course of the pendulous urethra, drying his field from time to time with an applicator, and accurately localize any granular patches which exist. These can generally be distinguished by the different texture of the tissues and by the loss of the normal lustre. It must, however, be admitted that these granulations are more frequently found by those who are expert in the use of the endoscope than by those who use it only occasionally. The granulations should be touched with nitrate of silver, from fifteen to thirty grains to the ounce, and generally after one or two applications marked improvement will be seen.

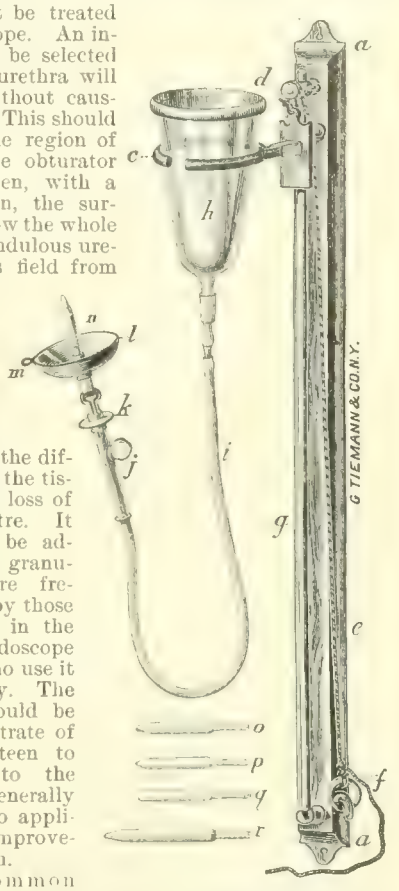


Fig. 4841.—Valentine Apparatus for Irrigating the Urethra and Bladder. The support for the apparatus is attached to the wall or to the woodwork of the room in such a manner that the bottom of the irrigator (*h*) is nine feet from the floor. The patient sits on a chair eighteen inches high. All irrigations are performed from this elevation; differences in the force of the stream are procured by drawing back or pushing forward the flange (*k*). *a, a,* board with brass rod (*g*); *c,* collar holding irrigator; *d,* pulley to raise irrigator for use or to lower it for cleaning and filling, but not for producing variations of force of stream; *e,* cord for drawing up irrigator; *f,* ring at end of hoisting cord; *g,* brass rod, serving as track for metal block which supports collar; *i,* soft-rubber tube six and one-half feet long; *j,* ring for fourth finger; *l,* shield for directing flow from urethra into basin on patient's lap; *m,* small ring for suspending stopcock when not in use; *n,* nozzle in place; *o,* pointed nozzle for normal meatus; *p,* dome-shaped nozzle for large meatus; *q,* flattened nozzle for small meatus; *r,* nozzle for irrigating female urethra and bladder.

Another common cause of a slight amount of discharge is to be found in the persistence of infection in the glands of the urethra. These can hardly be reached by local applications, and are best treated by stretching the urethra moderately with sounds or with a Kollman dilator. This should not be done more than once in five to seven days, and the urethra should be carefully irrigated with some mild antiseptic solution after instrumentation. The patient should also be given either one of the balsams or the oil of sandal-wood, which act extremely well in these chronic or subacute cases. The use of astringent washes, as permanganate of potassium, sulphate or sulpho-carbolate of zinc, and the like, is also useful, as the discharge is in part due to hypersecretion of a slightly injected mucous membrane, which will yield nicely to the use of astringents, either by injection or by irrigation.

Other Forms of Urethritis.—There still remain to be considered three other forms of urethritis, which are important chiefly because they are occasionally confounded with gonorrhœal urethritis. Such mistakes can hardly occur except where a diagnosis is to be made between the later stages of an acute urethritis and the earlier stages of these other varieties. An inflammation of the urethra coming on after a definite period of incubation, accompanied by a profuse purulent discharge and showing the presence of intracellular diplococci, can hardly be mistaken. It is not to be denied that there are other diplococci in the urethral discharges, and that they may occasionally stand in an etiological relation, but these are very rarely capable of producing a profuse discharge, with other symptoms of acute infection. When we have to deal with a so-called "gleety" discharge, showing the presence of diplococci, the diagnosis cannot be so easily made, and it is also true that even the use of Gram's stain is not sufficient to distinguish between these organisms, and cultural methods alone are to be regarded as absolute. When, therefore, the importance of an accurate diagnosis is extreme, no staining or morphological distinctions are to be regarded as absolute. The most important question which the practitioner is called upon to decide is the distinction between a fresh infection and the lighting up of an old gonorrhœal inflammation. As is well known, this tendency to recur is very marked, even after the lapse of months or years. A "flare-up," so called, may generally be distinguished by its rapid onset, showing little or no period of incubation, its comparatively mild course, and its tendency to subside under mild treatment. Gonococci will generally be present in considerable numbers at first, but they rapidly disappear. These cases are to be distinguished from the cases of so-called "simple urethritis," which are due to infections of the urethra with other organisms. It is now beyond question that other organisms are capable of exciting urethritis, but they act rather as a local irritant and differ markedly from a gonorrhœal infection. They show little or no period of incubation, the discharge as a rule is muco-purulent, and they subside in a few days, with or without treatment. If the discharge be examined under the microscope a variety of cocci and bacilli may be found, and possibly intracellular organisms. The infection is frequently not pure, and mixed cultures are generally to be obtained. It is of the first importance that these cases should not be confused with a true gonorrhœal infection, as serious consequences might follow such a mistake.

Treatment.—These cases do well under mild astringent or antiseptic irrigations, and are to be treated locally from the very start. As a rule they subside in the course of a week or ten days.

Chancroidal Urethritis.—The possibility of a chancroidal ulceration extending into the urethra as far as the fossa navicularis must be remembered. As a rule the diagnosis is accompanied by no difficulties, and the evidence of an ulcerative process generally extending out on to the glans will render the diagnosis easy. The treatment is that of chancroidal ulcers elsewhere.

Syphilitic Urethritis.—Intra-urethral chancres are not uncommon. Their presence is accompanied by a moderate purulent or muco-purulent discharge, which might be mistaken for an atypical case of gonorrhœa. Such errors may be avoided by palpation of the anterior urethra, which will show the presence of an indurated area, generally in the first inch and a half of the urethra. These are to be distinguished from peri-urethral abscesses, or so-called folliculitis, by their hardness, and by the absence of tenderness; often by their position at or near the meatus, and by the appearance of a roseola. The treatment is that of syphilis elsewhere.

STRICTURE OF THE URETHRA.

Strictures of the urethra may be congenital or acquired, but the vast majority of strictures with which the practitioner has to deal come under the latter heading.

Congenital Strictures.—Congenital strictures of the urethra are rare. They are generally at the meatus and may be of extremely small calibre.

The *etiology* is obscure. Cases of stricture further back than the meatus have been reported as congenital.

The most generally accepted theory in regard to the causation of hypospadias and epispadias is that they are due to intra-uterine stricture with rupture and sloughing. If this theory be accepted it will clear up the etiology of congenital stricture.

The *treatment* is that of stricture in the adult.

Acquired Stricture.—*Spasmodic Stricture.*—Under this heading we must consider the so-called spasmodic strictures, which, though not strictures in the narrowest sense of the word, are yet frequently productive of the symptoms of stricture. They are due to spasm of the muscular fibres in the urethra, producing more or less obstruction. By far the most common cause of spasm is a sensitive area due to inflammation, which may be sufficiently localized to be described as ulcer. This, when approached by an instrument, resents the interference, causing contraction of the muscular fibres and a consequent obstruction to the passage of the instrument. It may in this way give rise to signs closely resembling organic stricture, and is, to be distinguished largely by the history, which will as a rule show an entire absence of symptoms except when the urethra is examined with an instrument.

There are also cases of spasmodic stricture apparently of purely nervous origin. These occur in neurotic individuals, and are most pronounced when their nervous symptoms are prominent. The diagnosis is to be made only upon the history, an entire absence of inflammatory disease, and the demonstration of the absence of local areas of congestion. It is probable that, if put to this test, the number of spasmodic strictures of nervous origin will not be found large. Spasmodic stricture disappears under full surgical anæsthesia.

Organic Stricture.—The two prime causes of organic stricture are trauma and gonorrhœal urethritis.

Traumatic stricture has already been discussed under rupture of the urethra and will not be further mentioned here.

While it is not to be denied that urethritis of other than gonorrhœal origin is at times sufficiently severe to be capable of producing true organic stricture, cases in which such has actually occurred are extremely rare.

Pathology.—The trouble begins with the loss of a small portion of the mucous membrane, which results in the failure of the tissues to protect the deeper parts, and as a result they become infiltrated with urine. This sets up an inflammatory exudate in the submucous layer, with the deposit of fibrous tissue. It is stated upon good authority that the fibrous tissue here formed differs from scar tissue in other regions by showing a greater tendency to contract. This may be real or due to the fact that in many cases infiltration has taken place about the whole circumference of the urethra, and that a very moderate amount of contraction at any one part will produce a very decided contraction of the whole. It is also to be remembered that the process of formation is an extremely slow one, and, therefore, that the scar is laid down layer upon layer in the endeavor to protect the deeper parts from the extremely irritating urine which infiltrates it. In this way a concentric scar is formed, and we need not suppose any exceptional qualities in the fibrous tissue in order to show an extremely persistent tendency to contract.

Changes in Other Organs.

Changes in the Urethra.—The changes in the urethra itself due to stricture and yet not immediately at the point of stricture, are due to the fact that the urethra behind the point of narrowing is not completely emptied. The condition begins by the retention of a drop of urine behind the stricture—leading to irritation and frequently a slight discharge, which is often referred to as a "gleet."

This is nothing more than the attempt on the part of the mucous membrane to protect itself against the irritating properties of the urine. As the process goes on and the narrowing becomes more complete, there is dilatation of the urethra at this point, which may become extreme. With this dilatation goes a decrease in vitality of the tissues, with consequent maceration and perforation of the mucous membrane, leading to a small abscess, which may go on to the formation of a fistulous opening behind the stricture and in extreme cases to extravasation of urine. The abscesses and fistulæ thus formed may be multiple, and the cause of multiple fistula formation is not necessarily the presence of multiple strictures. Multiple fistulæ may and frequently do exist with but one stricture. This is due to the fact that, as the fistula becomes chronic, much fibrous tissue is deposited along its walls, which then contract and the fistula no longer serves to drain the cavity from which it started. The infection then extends in another direction, with the formation of a new fistula, and the process may go on until several are formed, giving rise to the condition known as "a watering-pot perineum."

Extravasation of urine is due to a rupture of the urethra behind a stricture, and differs in no way from that which occurs from traumatic rupture of the urethra.

Changes in the Bladder, Ureters, and Kidneys.—With the increasing obstruction in the urethra comes a hypertrophy of the bladder, with not infrequent sacculation, and unless this hypertrophy absolutely keeps pace with the obstruction there comes a time when the bladder is not completely emptied, and there is residual urine and a condition favoring cystitis. The number of cases in which some residual urine is to be found is probably much larger than is generally supposed, and is stated by some writers as high as sixty per cent. With the occurrence of residual urine of any amount there comes a back pressure upon the ureters and pelves of the kidneys, resulting in dilatation and thereby favoring infection not only of the ureter and pelvis, but also of the secreting portions of the kidney. In this way arise the conditions known as pyelonephritis, or "surgical kidney," rendering any surgical operation risky.

Varieties of Stricture.—It is customary to describe the anatomical characteristics of a stricture as one of three varieties.

A stricture which is extremely narrow and resembles a band constricting the urethra is spoken of as linear.

A wider band, which constricts a moderate amount of the urethra in a symmetric manner, is spoken of as an annular stricture.

A stricture of greater length, which has narrowed the urethra unequally in its different parts and has, therefore, pushed the portion of the canal which remains patulous first to one side and then to the other, is spoken of as tortuous.

These varieties are not of great importance in the treatment of stricture, for in some cases all three varieties may be present in one patient, and it is difficult, without the use of complicated apparatus, to decide exactly as to the particular class to which a given case belongs.

Strictures are also divided, according to their diameter, into strictures of large and strictures of small calibre. This is a distinction which, in the light of our present knowledge, might properly be abandoned. The term of "large calibre" was introduced by Otis and his followers, who regarded any narrowing of the canal below that calibre, established by an arbitrary scale, as evidence of stricture. To-day it is generally admitted that many so-called strictures of large calibre should properly have been regarded as physiological narrowings of the canal, and, as the term carries with it no important distinction, it should properly be abandoned. For practical purposes, only the strictures which were termed by Otis "strictures of small calibre" are to be regarded as organic strictures at all. It is always proper in describing a stricture to speak of it as a large or a small stricture, but when these expressions are used they are not intended to refer to the term "stricture of large calibre," which has come to carry with it an especial meaning, and is not to-day believed to be in accordance with the facts.

Location of Strictures.—There are three points in the urethra at which organic stricture is most commonly to be found.

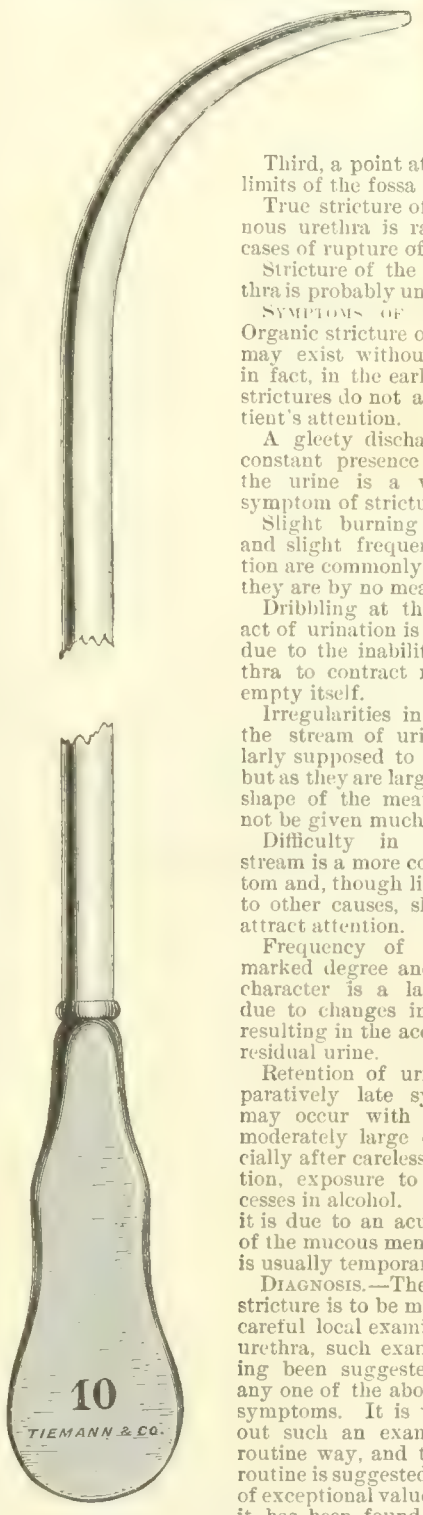


Fig. 4842.—Curved Steel Sound.

First, the region of the bulb.

Second, the region of the peno-scrotal angle.

Third, a point at the posterior limits of the fossa navicularis.

True stricture of the membranous urethra is rare except in cases of rupture of the urethra.

Stricture of the prostatic urethra is probably unknown.

Symptoms of Stricture.—Organic stricture of the urethra may exist without symptoms; in fact, in the early stages most strictures do not attract the patient's attention.

A gleety discharge with the constant presence of shreds in the urine is a very constant symptom of stricture.

Slight burning or irritation and slight frequency of urination are commonly observed, but they are by no means constant.

Dribbling at the end of the act of urination is common, and due to the inability of the urethra to contract regularly and empty itself.

Irregularities in the shape of the stream of urine are popularly supposed to be important, but as they are largely due to the shape of the meatus they need not be given much importance.

Difficulty in starting the stream is a more common symptom and, though likely to be due to other causes, should always attract attention.

Frequency of urination in marked degree and of constant character is a late symptom, due to changes in the bladder resulting in the accumulation of residual urine.

Retention of urine is a comparatively late symptom, but may occur with strictures of moderately large calibre, especially after careless instrumentation, exposure to cold, or excesses in alcohol. In these cases it is due to an acute congestion of the mucous membrane, which is usually temporary.

Diagnosis.—The diagnosis of stricture is to be made only by a careful local examination of the urethra, such examination having been suggested by almost any one of the above-mentioned symptoms. It is wise to carry out such an examination in a routine way, and the following routine is suggested, not because of exceptional value, but because it has been found valuable in practice:

Examination should be begun with a sound as large as the meatus will comfortably admit. If this is arrested a smaller size may be tried, but stiff instruments smaller than 18 or 20 F. cannot be regarded as safe. The presence of stricture having been ascertained with the sound, examination may then be made with the bougie à boule (Fig. 4843). The larger sizes of this instrument are likely to give confusing results, as it is difficult to distinguish physiological from pathological narrowings. With these instruments it is possible to locate the position of the stricture and its size, if it will admit them at all. They are not of much value in sizes smaller than No. 10 F., as the points become engaged in small pockets in the urethra. If sizes smaller than this are required, flexible bougies, either of the English webbing or the French make, are most valuable. With them the presence of organic stricture can be definitely ascertained by the peculiar gripping sensation felt as they are being withdrawn. This sensation is sufficiently peculiar to be distinctive if once felt. If soft bougies cannot be passed, resort must be had to the filiform bougies. These are extremely liable to be caught in the orifices of the ducts and glands of the urethra, and their use is a matter of some difficulty and belongs to the province of the specialist.

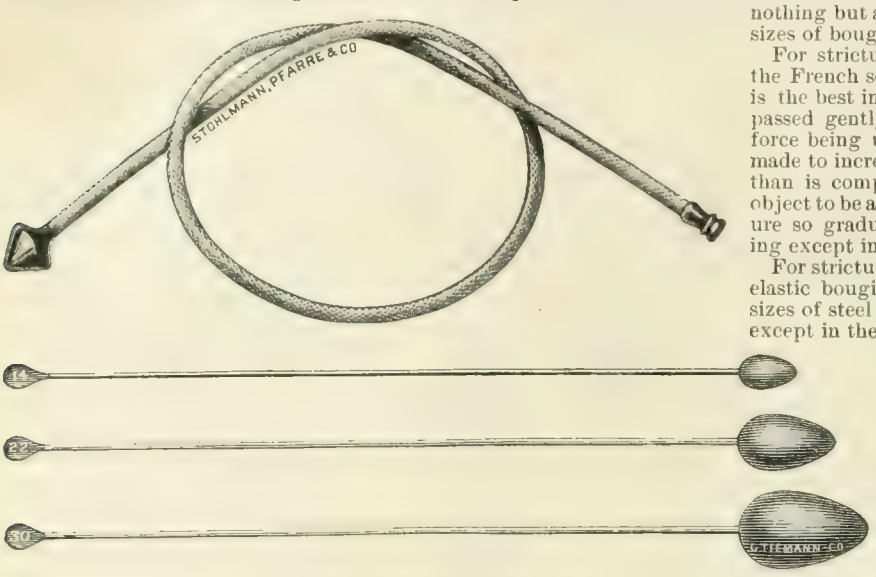


Fig. 4843.—Varieties of Bougie à Boule.

Fig. 4844.—Gum-Elastic Bougie.

Treatment.—The treatment of stricture of the urethra may be briefly considered under three general headings:

1. Gradual dilatation.
2. Continuous dilatation.
3. Urethrotomy, internal or external.

Gradual dilatation is the treatment of election in all cases above No. 10 of the French scale. In many of the more chronic cases it will fail and must be replaced by some more radical method, but an attempt at cure by this means is never out of place except in cases in which retention has either occurred or is threatened, or in which nothing but a filiform bougie or the small sizes of bougies can be passed.

For strictures of a calibre 18 to 20 of the French scale the conical steel sound is the best instrument. This should be passed gently through the stricture, no force being used and no attempt being made to increase the sizes more rapidly than is compatible with comfort. The object to be attained is to dilate the stricture so gradually as not to cause bleeding except in most moderate amounts.

For strictures below 18 F. the soft gum elastic bougies are safer, as the smaller sizes of steel sounds are deadly weapons except in the hands of the very expert.

Gradual Dilatation.—The possibility of dilating a stricture by the passage of instruments of increasing size depends upon the stirring up of a mild grade of inflammation in the stricture, thus promoting absorption and softening the scar. For this reason instruments should be passed at such intervals as give the best results in individual cases. The interval will vary from three to six or seven days, and the attendant should be guided by the facility with which the sizes can be increased. The average interval will be about once in five days. After dilatation has been carried up to 28 or 30 F. the interval should be extended as rapidly as possible without the occurrence of recontraction. In this way it may soon be increased from weeks to months, and a condition attained when the patient can either pass an instrument for himself, or visit his surgeon once or twice a year to see that the calibre has been maintained.

Any instrumentation should be followed by a thorough washing of the urethra, to remove as far as possible dangers of infection.

This form of treatment will fail in cases of old stricture with much scar-tissue formation, particularly those which bleed very readily, and in which each gain in size is accompanied by corresponding damage to the mucous membrane. If, after a moderate trial of one or two months, no notable gain has been attained, it is better to resort to some more radical form of treatment than waste further time in what is likely to prove a hopeless task.

There are also a certain number of what are known as "resilient strictures," which, though they can be dilated up to or above 20 F., cannot be kept at this figure except by constant treatment, and show a very marked tendency to recontract. Under these circumstances, after a fair trial of gradual dilatation, resort should be had to cutting operations.

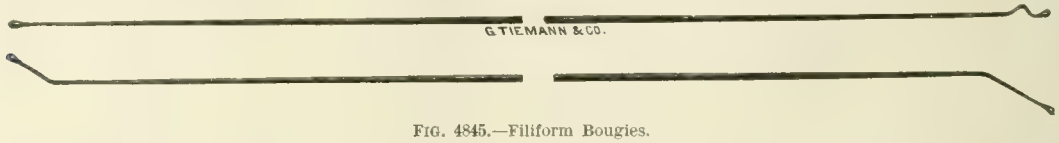


Fig. 4845.—Filiform Bougies.

Continuous Dilatation.—The term "continuous dilatation" is applied to a method occasionally applicable to strictures of small calibre, through which only the smallest instruments can be passed. It may be tried on any passable stricture before resorting to cutting operations, but is likely to prove successful only in a small number

of cases. A filiform bougie may be passed through the stricture and fastened in place. After the lapse of twenty-four to forty-eight hours it will be found that a larger instrument can be inserted. These small solid instruments in the urethra do not interfere with the passage of urine. By gradually increasing the size every few days, with the patient, of course, under constant observation, it may be possible to obtain a calibre sufficiently large to warrant the employment of gradual dilatation. It is to be remembered, however, that this treatment is applicable only to a small class of cases under constant observation, and requires considerable skill and an intimate knowledge of the treatment of stricture in order to be successful.

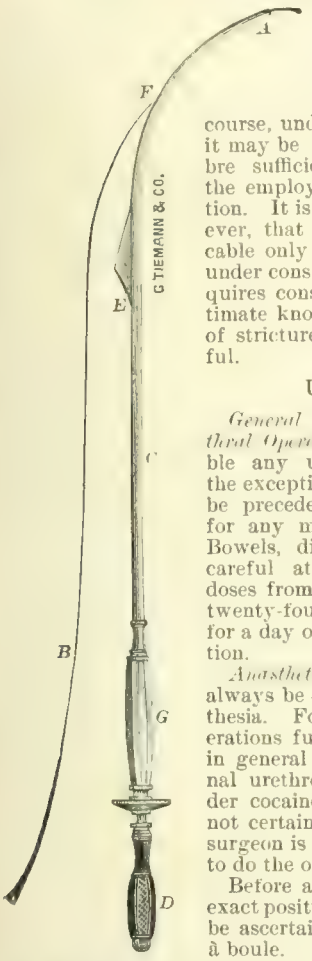


FIG. 4846. — Teevan's Modification of Maisonneuve's Urethrotome.

URETHROTOMY.

General Preparation for All Urethral Operations.—Whenever possible any urethral operation, with the exception of meatotomy, should be preceded by a preparation as for any major surgical operation. Bowels, diet, etc., should receive careful attention. Urotropin in doses from ten to fifteen grains in twenty-four hours should be given for a day or two previous to operation.

Anæsthetics. — Meatotomy may always be done with cocaine anæsthesia. For all other urethral operations full surgical anæsthesia is in general to be preferred. Internal urethrotomy may be done under cocaine, but the anæsthesia is not certain to be complete and the surgeon is likely to feel hurried and to do the operation less thoroughly.

Before any cutting operation the exact position of the stricture should be ascertained by means of bougie à boule.

The operations upon the urethra coming under the head of urethrotomy may be divided into two general groups:

INTERNAL URETHROTOMY AND EXTERNAL URETHROTOMY. — *Internal Urethrotomy.* — This procedure becomes the operation of election under the following general conditions:

1st. Stricture of the meatus. All narrowings of the meatus sufficient to be pathological are best treated by cutting operations, as dilatation in this region is likely to be both painful and unsuccessful.

2d. In strictures anterior to the bulb, large enough to admit the necessary instruments, under the following conditions:

(*a*) When gradual dilatation, tried for a sufficient length of time, has failed to give good results.

(*b*) In case of so-called "irritable strictures," namely, those followed by increased discharge, increase of spasm, urethral fever, etc.; also in the so-called "resilient strictures."

(*c*) The presence of urinary fistulæ and other suppurative peri-urethral complications not requiring perineal section.

(*d*) To admit the passage of instruments prior to operations within the bladder, as in litholapaxy or before operation on an enlarged prostate, to permit urethral drainage.

There are two general types of internal urethrotomy:

1st. The operation cutting from before backward. For this the Maisonneuve and modifications of this instrument (Fig. 4846) serve as a type. Briefly described, the operation is as follows:

A filiform bougie is passed through the stricture and the instrument is then attached to this as a guide. The shaft is passed down to the anterior face of the stricture and the knife is then pushed forward until all stricture tissue has been divided. The knife is then withdrawn into its sheath, the instrument removed, and a bulbous bougie or sound passed to ascertain that all the scar tissue has been divided. The objection to operations of this type are that it is difficult to divide the whole thickness of the stricture, and consequently the cutting has to be repeated.

2d. Operation cutting from behind forward.

In this country the instrument invented by Otis, and Wyeth's modification of the same, are much more generally used. These do their cutting from behind forward.

The Otis urethrotome is passed until the cutting blade is half an inch behind the posterior face of the stricture. The instrument is then screwed open until the stricture is put upon the stretch, when the knife is withdrawn so as thoroughly to divide the scar tissue. The instrument is then further screwed open in order to insure full dilatation at the point of incision. A full-sized sound should then be passed in order to ascertain whether or not the calibre of the urethra is normal. This operation is applicable to any part of the urethra anterior to the bulb.

In the portion of the urethra between the bulb and the posterior limits of the fossa navicularis all cutting should be done on the roof in the median line. Strictures in the fossa and at the meatus should be cut upon the floor. Strictures behind the limits above mentioned should not be treated by internal urethrotomy except when combined with external, on account of the danger of wounding large vessels and giving rise to primary or secondary hemorrhage. In all operations within the urethra, except at the meatus or of very minor degrees, it is wise to tie in a catheter for the first day or two. This serves the double purpose of preventing hemorrhage and avoiding a possibility of infiltration of urine.

Meatotomy.—Operations within an inch of the meatus may be done with a blunt-pointed straight bistoury, and, as above mentioned, all cutting should be upon the floor. If preferred, the Otis instrument may be used in the reversed position.

External Urethrotomy.—External urethrotomy becomes the operation of election for the great majority of all strictures at or posterior to the bulb, which require anything more than gradual dilatation. It will be seen, therefore, that the operations anterior to the bulb are amenable to internal, those posterior, to external urethrotomy. This operation is particularly adapted to tight strictures of the bulbous portion, with or without urinary fistulæ; to traumatic stricture; and to all so-called impassable strictures. The type of operation in external urethrotomy will vary with the possibility of passing a guide through the stricture. It has become customary to speak of all operations done with a guide

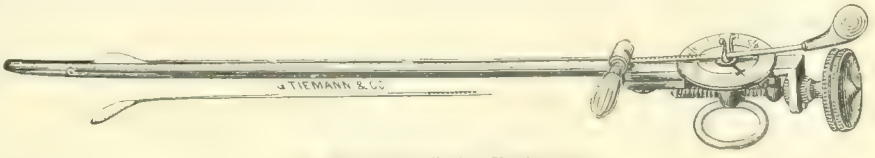


FIG. 4847. Otis Dilating Urethrotome.

as simply "external urethrotomy." When no guide can be introduced the term "external urethrotomy without a guide," or perineal section, is generally adopted.

External Urethrotomy with a Guide.—All the precautions above mentioned with regard to the preparation of the patient and location of the stricture should be observed. Full surgical anæsthesia is necessary. The operation most generally done is that modelled after the operation originally described by Syme. It is briefly as follows:

The patient is placed in the lithotomy position. A grooved guide is passed, care being taken to ascertain that it has entered the bladder, and is held strictly in the middle line. The knife is then introduced in the middle line of the perineum, about half or three-quarters of an inch in front of the anus or behind the stricture. With the blade of the knife turned upward, it is pushed rapidly forward until it strikes the groove of the guide, when the cut is continued upward, completely dividing all stricture tissue from behind forward. The guide is then withdrawn and a full-sized sound passed to make sure that the stricture is completely divided. This is withdrawn and a catheter is tied in place in order to drain the bladder and form a smooth surface around which the wound may heal. In regard to the length of time during which this catheter should remain in place much difference of opinion exists. Many of the best authorities advise that it should be removed after two or three days, long before the wound is healed and while urinary leakage will still occur freely. It has seemed wiser to me to leave the catheter in place for a week or ten days, or even two weeks, until the wound is nearly closed. It may be necessary to remove the first catheter and replace it by another, but I believe that smooth healing without complication is more likely to be obtained by the adoption of this course than when the catheter is removed in a few days and the urinary fistula allowed to close as best it can.

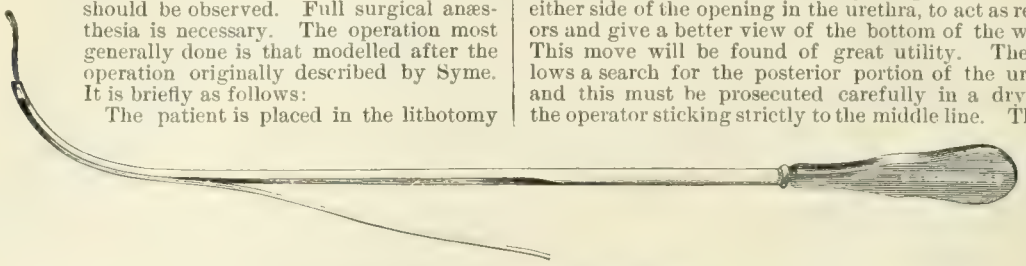


Fig. 4848. Gouley Tunnelled, Grooved Guide.

Fig. 4849. Wheelhouse Staff.

External Urethrotomy without a Guide.—Perineal Section.—This operation is among the most difficult and tedious of the operations of surgery. It should never be undertaken except by a surgeon who is prepared for a major operation. The best light, the best assistance, and the best surroundings should always be secured. Before deciding to do the operation without a guide a painstaking attempt should be made to pass a filiform bougie through the stricture, for, if this can be done, the operation is converted instantly from one of great difficulty to one of perfect simplicity. Attempts to pass an instrument having failed, two courses are open, one by far the best: to open the urethra in front of the stricture and attempt to find the opening in the stricture (Wheelhouse operation), or the knife may be boldly plunged into the apex of the prostate behind the stricture and the urethra opened at this point (Cock's operation).

Wheelhouse Operation.—For this operation a special straight grooved staff terminating in a hook, invented by Mr. Wheelhouse, is frequently used (Fig. 4849).

With the patient in the lithotomy position, this staff, with its groove upon the floor of the urethra, should be passed down to the face of the stricture. It is then intrusted to an assistant, to be held strictly in the middle line, and the urethra is opened at the point where the staff shows the face of the stricture to be. The staff is then turned so that its hooked extremity catches the upper angle of the wound and draws it upward. Mr. Wheelhouse advises the placing of guide stitches in either side of the opening in the urethra, to act as retractors and give a better view of the bottom of the wound. This move will be found of great utility. Then follows a search for the posterior portion of the urethra, and this must be prosecuted carefully in a dry field, the operator sticking strictly to the middle line. The orifice will frequently be found nearer the roof than the floor and every likely pocket should be searched with a probe until the right one be found. If the bladder be distended with urine, pressure with the hand above the pubes may force a few drops of urine out at the opening, thus giving the key to the situation. Time, patience, and a good light are the prime requisites to success, but in the most skilful hands hours may be consumed in the search. In case of failure, after prolonged search, the bladder may be opened above the pubes and an instrument passed through the urethra from behind forward, or Cock's operation may be done. I am inclined to believe that suprapubic cystotomy and retrograde catheterization is an operation which has been too much dreaded, and that it may frequently be done without running a risk so great as that taken by a prolonged and fruitless search for the urethra. When the orifice has been found, a probe-pointed gorget or grooved director should be passed to the bladder and the stricture divided along the floor or dilated with a proper dilator. After this a full-sized steel sound should be passed to the bladder, it being made to turn the corner at the urethral opening with the assistance of the gorget. This having been done, the bladder should be washed out and a catheter tied in place to secure permanent drainage. Some authorities advise the drainage of the bladder with a perineal tube brought out at the perineal wound and left in position for a few days. I believe that, except in cases complicated with abscess formation or enlarged prostate, an in-lying catheter will secure sufficiently good drainage and promote a more rapid healing of the wound.

Cock's Operation.—This operation may be dismissed with the comment that to plunge a knife blindly into the tissues in order to open a urethra, the position of which is uncertain, is not to-day a sound surgical procedure.

Miscellaneous Methods of Operation.—*Divulsion.*—The operation of divulsion, though still practised by some of the best genito-urinary surgeons, hardly comes up to the standard of modern accuracy. It is impossible to tell in exactly what direction the splitting force will be exerted, and the rent may occur in an undesirable place. It seems to have no obvious advantages over a carefully practised internal urethrotomy, and is capable of giving bad results through the formation of excessive scar tissue.

Fig. 4850.—Probe Gorget.

Excision.—A considerable number of surgeons have

practised the operation of excising well-localized strictures through a perineal opening. These have been treated by an attempt to bring the ends of the urethra together, by grafting, and by plastic operations. In some of the best cases, however, the ends of the urethra have been left separated and allowed to granulate up over an in-lying catheter. The operation appears to have given excellent results in properly selected cases.

Electrolysis.—The application of electricity to the absorption of strictures has been enthusiastically advocated from time to time. Its advocates have, however, generally been enthusiasts whose results have not been verified by general experience, and it may be confidently asserted that electricity cannot be expected to cure organic stricture of the urethra.

Prognosis of Operative Treatment of Stricture.—Internal urethrotomy is frequently referred to as a trivial operation, devoid of danger. This statement, however, cannot be allowed to stand in the face of statistics, and a practitioner advising the operation must reckon with a mortality in the vicinity of two per cent., when all cases are taken into consideration. While this is not a large mortality, it is sufficiently important to emphasize the necessity of doing the operation only when it is distinctly indicated.

Uncomplicated cases of external urethrotomy should not have a mortality higher than that of internal urethrotomy. The possibility of complications is, however, considerable, as the strictures of the deep urethra, to which this operation is applicable, are more likely to have affected the other urinary organs, thereby increasing the risk of any surgical operation.

Perineal section is an operation of considerable mortality, which cannot be accurately stated, but is probably in the vicinity of fifteen per cent. This is due to the fact that the cases are much less favorable for operation on account of the frequency of pyelitis and pyelonephritis, and the mortality is not directly due to the operation itself, but to conditions antedating the operation. It must, however, be considered as a distinctly dangerous operation, but the mortality should never deter a properly qualified surgeon, as the conditions which call for it are certain either to prove fatal or to leave the patient in a condition less favorable for operation.

Results of Treatment.—The ultimate results in the treatment of stricture of the urethra may be considered from two points of view:

1st. As affected by the position of the stricture, and

2d. By the method of treatment.

Position of the Stricture.—In general it may be said that the outlook for radical cure decreases with the distance the stricture is situated from the meatus. Stricture at or near the meatus, if treated by a proper cutting operation, is practically alway sentirely relieved. Strictures of the pendulous urethra can generally be radically cured. Strictures of the bulbous and membranous urethra generally require the more or less continuous use of instruments in order to maintain a full calibre.

Method of Treatment.—Gradual dilatation will radically cure a certain number of cases of stricture of the anterior urethra. The exact proportion cannot be accurately stated, but in the majority of cases the full calibre of the urethra is maintained only by the occasional passage of instruments.

Internal urethrotomy is more likely to produce radical cure in properly selected cases of stricture of the anterior urethra. The percentage of cures cannot with certainty be stated at over fifty per cent., and in extensive or narrow strictures it is not notably more successful than gradual dilatation.

External Urethrotomy and Perineal Section.—Strictures of the deep urethra requiring external urethrotomy or perineal section are rarely, if ever, radically cured by operation. A certain amount of recontraction is to be expected, and permanent cure should never be promised to the patient, though it may occasionally result. The old saying, "Once a stricture always a stricture," is nowhere more applicable than to the deep urethra.

Complications of Stricture of the Urethra.—The most serious complication requiring surgical treatment is abscess formation and infiltration of urine. The direction which the septic processes will take has been already described under the section on rupture of the urethra. Where the rupture takes place owing to an organic stricture of the urethra, the process is likely to be more insidious in its onset, but none the less disastrous in its consequences. Extreme destruction of tissue in the region of the bulbous and membranous urethra and in the loose tissue of the scrotum occasionally takes place. The treatment should consist in free incision and drainage of all accessible infected areas, together with relief of the stricture.

Hemorrhage.—Hemorrhage in operations for stricture of the urethra, either internal or external, is rarely serious. When occurring in internal urethrotomy it can be efficiently controlled by the passage of a full-sized catheter to the bladder, followed by pressure along the urethra against the catheter. This can sometimes be exerted by a T-bandage, pressing the parts snugly against the pubes, or by winding a narrow bandage or strip of adhesive plaster about the penis.

Hemorrhage following external urethrotomy can be controlled by pressure or by packing the wound. Care should be taken to ascertain that leakage is not going on backward into the bladder, as evidenced by the occurrence of clots in the urine coming through the catheter, or by failure of the catheter to drain. Should the hemorrhage taking place in this direction be alarming, it may be controlled by the distention of the deep urethra with a perineal tube, combined with packing the wound. These hemorrhages may be primary or secondary, and are rarely of serious note.

Septicæmia.—It is extremely rare to-day that serious general infection follows operations upon the urethra except where rupture of the urethra or abscess formation has already occurred. Much of the improvement is probably due to the use of urinary antiseptics, of which urotropin is at present the most valuable. However, in isolated cases extremely virulent streptococcus infections occur, which are as a rule rapidly fatal. Treatment should be addressed to supporting the patient's condition, and will probably have little effect upon the result. *Hugh Cabot.*

URICIDIN is a granular salt containing the sulphate, chloride and citrate of sodium, the citrate of lithium, and other salts. It is made by adding 20 parts of sulphuric acid and 4 parts of hydrochloric acid to sufficient clarified lemon juice to represent 50 parts of citric acid. This is then nearly neutralized with sodium bicarbonate, 1 part of lithium carbonate is added, and it is evaporated down and granulated. It is employed in teaspoonful doses in gout and rheumatism. *W. A. Bastedo.*

URINARY BLADDER, EXTIRPATION OF.—History.—The first operation for removal of the bladder was made by Bardenheuer, in 1887, in the male. The first operation in the female was made by Pawlik, in 1888. Since that time more than a hundred cases have been operated upon. In this country the operation has been done by many different surgeons, both in the male and in the female. In the female, Martin, of Chicago, was the first to operate, his first operation being in 1892. The bladder was removed with a uterine fibroid. He has also operated on several other cases. Mann,* of Buffalo, has operated on three cases, the first one in 1900. C. C. Frederick, of Buffalo, E. Reynolds, of Boston, and A. Lapthorn Smith, of Montreal, have each operated once. The operations upon the male for exstrophy have been quite numerous.

Indications.—The indications for the performance of this operation are: first, incurable disease of the bladder, such as cancer and tuberculosis; second, exstrophy; third, incurable disease of surrounding organs which has begun

* Trans. Amer. Gyn. Soc., 1901.

to involve the bladder, such as cancer of the uterus in the female.

Management of the Ureters.—In the male the method generally proposed has been the grafting of the ureters into the bowel. In 100 cases collected by Bovée the ureter was grafted into the bowel separately 31 times; by the Maydl and Pozza method, 44 times; into the urethra, 13 times; into the vagina, 8 times; and into the skin, 4 times. This is the most important question connected with the operation, and must be clearly understood. As the conditions in the male and the female vary very much, different methods may be used in the two sexes. I will, therefore, first consider the methods in the male.

The first plan used by Bardenheuer was to insert the cut ends of the ureters directly into the rectum. Experimentation upon the lower animals, by Peterson and

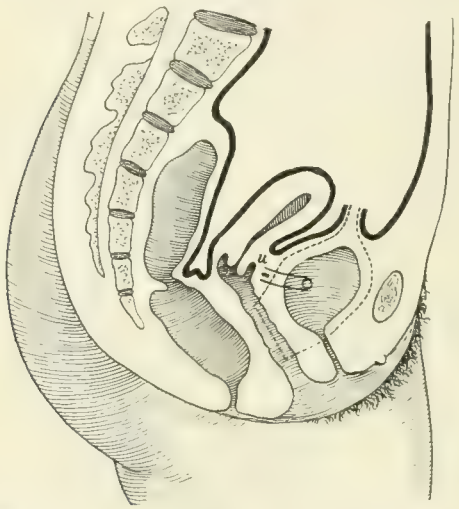


Fig. 4851.—Extirpation of the Bladder. The dotted line shows line of incision. The ureter (u) is roughly shown entering the bladder.

others, shows conclusively that this is an exceedingly dangerous method, as in almost every case, within a comparatively short time, infection travelled from the bowel to the kidney, and the animal died of this complication. The same thing has been noted in man, and the method is now considered so dangerous as to be practically given up.

Maydl proposed the removal of the trigone of the bladder with the ureters, and the transplantation of this piece of the mucous membrane of the bladder directly into the intestine. The results of this have been very much better, as the natural valvular action at the end of the ureters seems to prevent the ingress of infecting germs; so that many cases in which this has been performed have been permanently successful. This can only be done in cases in which the trigone is healthy, so that in exstrophy of the bladder it is the only recognized method. In the case of malignant disease and of tuberculous disease, which are most apt to affect the posterior wall of the bladder, it may be impossible to dissect out the trigone; in which case it will be necessary to put the cut ends of the ureters into the intestine. But, as this is almost certainly fatal, it would seem to rule out operations for removal of the bladder for these indications in the male in a large proportion of cases.

In the female we have the choice of two methods, both of which have been proved to be successful. We may either open the ureters into the vagina by a previous operation, as was done by Pawlik, or we may leave the cut ends of the ureters opening into the vagina after the removal of the bladder—methods which really amount to the same; or we may perform the operation of Maydl, or, better still, its modification by Pozza.

Pozza's operation differs from Maydl's in that more of the mucous membrane of the bladder is removed, and the trigone is not retained in one piece, but is divided by making a longitudinal median incision before separation. The results of both the Maydl and Pozza operations have been most satisfactory. Out of forty-four cases only two died of infection.

The grafting of the ureter to the skin has been done ten times, but the results are not encouraging. Sonnenberg implanted the exposed ureter of an ectopic bladder into the urethra of the glans penis. In all, more than twelve cases have been done by this method. It leaves dribbling of urine, but this is more easily taken care of than is grafting to the skin.

In the female, when the bladder is removed, by removing at the same time a portion of the anterior wall of the bladder the cut ends of the ureters may be left entirely alone; and, when cicatrization has taken place, they will be found to empty into the vagina. This gives an opportunity of making a receptacle for the urine out of the vagina by simply closing the vaginal entrance. As the urethra must also necessarily be cut in removing the bladder, it also will open into the vagina, and the patient will be able to empty the vagina through the urethra, either by the catheter or by voluntary effort, as was done in Pawlik's case. If the vagina is maintained in an aseptic condition during healing, ascending infection will be prevented. After complete healing of all the parts the danger of infection will be very greatly diminished.

In exstrophy of the bladder, in the female, the Maydl or the Pozza operation may be done on the vagina, thus obviating the necessity of opening the abdomen.

The Mauclaire-Gersuny operation consists in implanting the ureters into the rectum, which is cut off from the bowel above after an artificial anus has been made. Gersuny modified the original operation by bringing the bowel exit into the sphincter ani, thus doing away with the artificial anus and maintaining a separate receptacle for the urine.

Technique.—*Exstrophy in Men.*—The trigone is first dissected out with the ureters. The abdomen is then opened and the trigone carried into the rectum through an incision and sewed in place. After this the bladder is removed and the opening closed. The incision may be made curved, with its concavity downward from one inguinal canal to the other; a vertical incision may be made which can be enlarged by a transverse incision crossing the lower end of the vertical one.

In women the Pozza operation will be necessary, in order to get around the uterus. If it is desired to transplant the ureters into the vagina, a transverse incision may be made down to the peritoneum. After the trigone has been dissected out, the vagina can be pushed up by an assistant and opened and the trigone inserted. It will be necessary to dissect off the mucous membrane of the vagina on the anterior wall beforehand, so as to make a raw surface to which the trigone can adhere. The closure of the vagina can be left to a later date.

Cancer or Tuberculosis in the Male.—Although the indication may seem to be urgent, so far the technique of the operation is not complete enough to warrant its performance unless the parts around the bladder are healthy. This can be satisfactorily ascertained only after the bladder is opened. Suprapubic cystotomy must first be performed, and the bladder carefully examined. If the trigone be healthy, the abdomen must then be opened by a free longitudinal incision, the bladder thoroughly disinfected and laid open, and the trigone may then be dissected out (the patient being in the Trendelenburg position), with the ureters, and put into the rectum; after which the bladder may be easily removed, mostly by blunt dissection.

Cancer or Tuberculosis in the Female.—Owing to the fact that the ureters may be left undisturbed in the female, the operation is much easier than in the male. After the bladder has been carefully washed out, a median abdominal incision is made, and the patient put

in the Trendelenburg position, self-retaining retractors being introduced. The peritoneal covering is then incised over the bladder from side to side. The bladder is afterward loosened with the finger down to the attachments of the base, so that it is held only by the urethra, ureters, and attachments to the anterior wall. These are then cut with strong scissors, so as to remove a portion of the anterior wall of the vagina as big as a fifty-cent piece. Any bleeding vessels are tied and the peritoneum closed over the seat of the bladder with catgut suture. If the patient be in good condition, and no previous infection of the bladder exists, the vaginal entrance may then be closed by a plastic operation.

After-Treatment.—In order to keep the urine aseptic, and thus prevent ascending infection of the ureters, in all these operations it is well to give the patient large doses of benzoate of ammonium, beginning a few days before the operation. In women the vagina must be kept well cleansed out and drained. If the vagina be closed at the time of the operation, a self-retaining catheter should be passed through the urethra and left, the vagina being washed out through the catheter at least twice a day.

Results.—Bovée has collected 100 operations. Of these the operation was done 21 times for malignant disease, 3 times for tuberculosis, once for epispadias, once for fibroid of the uterus, and 5 times for conditions not noted.

In exstrophy Maydl's operation was done 38 times, with 8 deaths; Pozza's operation, 4 times—no deaths; anastomosis of the ureters into the rectum, 10 times, with 3 deaths; and separate anastomosis into sigmoid, twice, both patients dying. Sonnenberg's operation was done 13 times—no deaths.

For malignant disease 21 operations were done, with 11 deaths.

In 7 the ureters were grafted into the vagina, with 1 death from collapse, and 1 from peritonitis on the ninth day.

For tuberculosis, 3 cases, with 2 deaths, are reported.

Altogether there were 26 deaths in 100 cases. Sixty-nine operations for exstrophy gave 19 per cent. mortality, and 31 operations for other conditions gave 42 per cent. mortality. *Matthew D. Mann.*

URINARY SEDATIVES.—The conditions which require the use of urinary sedatives may be dependent upon some state of the urine itself or upon something entirely independent of it.

1. Certain drugs may cause intense irritability of the whole urinary tract—as, for example, cantharides and turpentine. A very acid urine or one containing crystals of uric acid or of calcic oxalate may give rise to symptoms of irritation. Again, a decomposing urine may produce similar effects. An alkaline urine, especially when associated with phosphaturia, may also give rise to discomfort.

2. We may begin at the kidney and find an occasional exciting factor outside of the urine itself, even as far down as the meatus. Pyelitis is a frequent cause, as are cystitis and vesical calculus. In women a uterus which is anteverted pushes into the bladder, while a retroverted uterus may pull upon that same viscus. Pelvic tumor, either prostatic in men or of the various kinds to which women are liable, may diminish the size of the bladder by direct pressure, or by traction, to such an extent that the desire to empty it is very frequent. Tumors of the bladder have a similar effect at times, though in these cases the sense of a foreign body in the bladder seems very often to furnish the stimulus. Stricture of the urethra seldom gives signs of urinary irritability until, in the process of contraction, it has reached such a small calibre that there is back pressure in the bladder. Finally, an adherent and tight foreskin is a well-known cause of occasional nocturnal, or even diurnal, incontinence, in children. We have thus very briefly suggested the more frequent causes of urinary irritability, as we can only hope for relief in a given case by carefully studying out the exciting factor. No good can be gained and much harm may be done by trying to cure all cases with any one remedy.

3. To the two classes of irritability mentioned we must add a third, in which we can find no tangible stimulus, and have to fall back upon a purely nervous origin for the affection.

Many remedies which have in the past been considered valuable in these cases have in recent years fallen into disuse; some deservedly as of little value, others through having been supplanted by more powerful drugs, acting in the same manner and more convenient to use.

As regards the cases which are due to some condition of the urine itself, an excessively acid urine can be rendered less irritating either by increasing the ingestion of liquids, and so diluting it, or by giving one of the alkalies. The citrate or acetate of potassium is most useful in these cases. Few patients will drink enough water unless given specific directions. Each of the salts named, when given in fairly large doses, has the effect of producing thirst and thereby making it easier for the patient to take enough water, while at the same time it renders the urine alkaline. Care should be taken not to make the urine too alkaline, lest we get a deposit of phosphates. If we are confronted by an excessively alkaline condition of the urine, it can be corrected by giving a drug that will change the reaction. The mineral acids are of little or no value for this purpose. Benzoic acid is useful. Given as benzoate of sodium, by the mouth, it is excreted in the urine as benzoic acid, which, besides the effect of rendering the excretion acid, also exerts an antiseptic effect. Ten grains given in a glass of water three times a day is usually enough. Urotropin makes the urine acid, and causes rapid disappearance of the phosphates in cases in which they are deposited in alkaline, neutral, or slightly acid urine. Five grains, given well diluted twice a day, is an ordinary dose. It is particularly valuable in the cases in which the urine is alkaline from decomposition, as it is broken up in its passage through the body, and the formalin which is set free is eliminated by the kidneys. In these cases the dose may have to be considerably increased. The bactericidal action of this remedy is marked. Boric acid in sufficient doses will render the urine acid, but it is less well borne by the stomach than are the remedies mentioned. Salol will give an acid urine, and is often of value, especially in cystitis.

In cases in which the irritability is due to crystals of uric acid or of oxalate of lime, measures looking to the elimination of the source of the crystals are needed. The usual antirheumatic remedies will remove the excess of uric acid. At times there is much difficulty in preventing the formation of oxalate-of-lime crystals. In the obstinate cases, in which other methods fail, one or two drops of strong nitro-muriatic acid, taken after meals in a full glass of water, will relieve the difficulty.

A careful regulation of the diet is of great importance in these cases. The amount of meat should be restricted when the uric acid is in excess. It should be borne in mind that fruit at times, and rhubarb often, cause an excess of calcic oxalate in the urine. Hæmaturia has been known to follow after eating rhubarb, so great was the irritation caused by the calcic oxalate crystals.

In case the discomfort comes from the use of certain drugs, as cantharides or turpentine, the omission of the medicine would at once suggest itself.

Alcohol is always contraindicated in any inflammation of the genito-urinary tract, and we often see the first serious symptoms, in a prostatic or stricture case, follow the ingestion of even a moderate amount of alcohol. A source of irritation which is often not considered is ginger ale. This is especially harmful in gonorrhœa, and I have seen a severe exacerbation follow its use. Under the same conditions highly spiced foods, such as curries, Welsh rarebit, etc., should be carefully avoided.

Pyelitis, whether of tuberculous or of some other origin, must needs be treated by drugs; some medicine must be used which is eliminated by the kidneys. Of these, prob-

ably all owe their value almost entirely to their antiseptic action. The remedies promising most are urotropin, buchu, uva ursi, pareira brava, and chimaphila. Urotropin is best given in doses of five grains three times a day. The dose of the fluid extract of each of the other drugs mentioned is a teaspoonful, well diluted, three or four times a day. These all have a slight antiseptic action, as shown by the diminished tendency to decomposition when the urine is left standing. This is particularly true of urotropin, but in very large doses it may cause some frequency of urination by rendering the urine too acid. Uva ursi has some diuretic action, as has also chimaphila. Buchu does not increase the amount of urine appreciably. In the very chronic form the stigmata of Zea Mays will be found a more effective remedy, as they stimulate the renal epithelium directly. A teaspoonful of the fluid extract may be given every four hours. In rare cases, in which something stimulating is required, small doses of turpentine may be of value. If the pyelitis be associated with renal calculus, a surgical operation, with removal of the stones and temporary drainage of the kidney, offers the best hope of permanent relief. By correcting the reaction of the urine we may prevent any increase in the size of the stones, but the chance of causing them to dissolve is remote. Hyoscyamus, phenacetin, belladonna, and opium in its various preparations, afford temporary relief. Sweet spirits of nitre at times helps and may relieve the vesical tenesmus, which is often associated with this disease. In tuberculous cases there is little hope of permanent relief except through nephrectomy or through the breaking down and complete disappearance of the organ, in consequence of which it will cease altogether to secrete any urine. In these cases the pain is often referred to parts of the urinary tract which are situated lower down and which are not involved in the disease.

In the cases due to diminution of the size of the bladder from extraneous causes the removal of those causes at once suggests itself. In prostatic hypertrophy the flow from an overdistended bladder may easily be mistaken for abnormal frequency of urination. This possibility should be investigated before seeking for a further cause. Overdistention may also occur in connection with a stricture of small calibre. Drawing off the residual urine under the strictest aseptic precautions one or more times daily may entirely relieve the symptoms. The administration of five grains of urotropin three times a day diminishes the danger of cystitis. In cystitis an antiseptic which will be eliminated in the urine is indicated. In many cases washing out the bladder once or twice a day with an antiseptic solution, such as a four-per-cent. solution of boric acid, is necessary. When stronger antiseptic washes are needed, one of permanganate of potassium or of citrate of silver will be found serviceable. Nitrate of silver is more stimulating and should seldom be used in solutions of more than one grain to the ounce. Pareira brava is said to be useful in chronic catarrh of the bladder. It checks bleeding in these cases and diminishes the muco-purulent secretion. Cubebs, copaiba, and sandal-wood, though more effective in irritation of the urethra, exert their influence through the medium of the urine and are of use in bladder affections. This is especially so of the oil of sandal-wood. All of these drugs resemble each other closely. It should be borne in mind that while they are being taken the urine is somewhat irritating. When they are given in large doses, they give rise to a constant desire to urinate, and the pain and difficulty in doing so are great. In some cases, in which the bladder and urethra are much inflamed, the pain may be so great as to lead to complete retention. The ordinary dose of each of these drugs is ten minims three times a day. They are best given in capsules, as the taste is disagreeable. Even in doses of ten minims twice a day the oil of sandal-wood at times gives so much backache that it has to be discontinued.

For the relief of the pain and frequency of urination associated with the presence of a calculus in the bladder, operation alone is of any avail. Morphine or belladonna or a combination of the two may afford great temporary relief.

At times we are forced to abandon our search for a tangible cause and fall back upon a neurosis as an explanation of the trouble. Here we may expect relief from the use of nervous sedatives, such as one of the bromides or hyoscyamus. Treatment of the condition through the urine proves as a rule unsuccessful, and washing out the bladder often only aggravates the patient's suffering. In the tenesmus of tuberculosis washing the bladder is generally worse than useless, especially if we have to pass a catheter for this purpose.

In the cases in which we need urinary sedatives, when the cause lies in the urethra itself, copaiba, sandal-wood oil, and cubebs give great relief. In the intense burning which accompanies micturition and which does not yield to internal medication or local treatment, the injection into the urethra of a two-per-cent. solution of cocaine alleviates the distress temporarily. In men, urination with the penis submerged in water as hot as can be borne, often gives relief.

Finally, in those cases of incontinence in children in which the trouble does not yield to belladonna in full doses, and appears to be caused by an irritable bladder, circumcision at times effects a cure.

Franklin G. Balch.

URINE.—Physical Properties. Quantity.—The amount of urine voided is dependent (1) on the state of the renal epithelium; (2) on the rapidity of the blood flow through the kidneys. It is independent of the blood pressure.

A normal healthy adult of the average weight of 75 kgm. passes from 1,500 to 2,000 c.c. of urine in twenty-four hours. Infants pass absolutely less, but, in proportion to their body weight, relatively more urine; this is largely due to the liquid diet. Abundant ingestion of fluids increases diuresis (*urina potus*); sweating (violent exercise, hot weather) decreases it. Less urine is normally passed at night than during the day; in chronic nephritis this ratio may be reversed.

Pathology.—Destructive renal lesions or local circulatory disturbances, in order to influence the flow of urine, must be bilateral; unilateral interference with diuresis is compensated by the healthy organ.

(*a*) *Polyuria.* The more chronic the nephritis the greater the tendency to polyuria (contracted kidney, amyloid). This is chiefly due to the contraction of the renal tissues and the resulting acceleration of the blood flow. During convalescence from acute nephritis; in heart and lung disease as soon as the circulatory disturbances begin to be compensated; in diabetes mellitus, and insipidus; after psychic shocks, and in various neuroses (*urina spastica*); after the exhibition of certain drugs (see *Diuretics*), and after the ingestion of certain articles of food (tea, coffee, alcohol, etc.)—the flow of urine is increased.

(*b*) *Oliguria.* In acute nephritis, in acute exacerbations of chronic nephritis, and in heart and lung diseases leading to stasis the flow of urine is decreased.

(*c*) *Anuria.* In uræmia (occasionally), in diseases causing great loss of fluids through other emunctories than the kidneys (acute gastritis and intestinal catarrh, with profuse vomiting and diarrhœa, cholera, dysentery), in rapidly progressive forms of anæmia, and in hysteria, the urine may be altogether suppressed.

Determination.—The urine should preferably be collected from morning to morning before eating; the bladder should be emptied before the collection is begun; the patients should urinate before going to stool, as, particularly in old women, much urine may be lost during the act of defecation. The total quantity may be measured or determined by weighing; the weight multiplied by the specific gravity yielding the volume. For clinical purposes the former method is best; for exact determinations the latter is to be preferred.

The Specific Gravity.—The specific gravity of the urine is, as a rule, high when little urine is voided and

low when the flow of urine is abundant. The same factors, therefore, that determine physiological fluctuations in the amount of urine also determine corresponding fluctuations in its specific gravity. As the normal total quantity varies from 1,500 to 2,000 c.c., so the normal specific gravity varies correspondingly from 1.025 to 1.015.

The specific gravity of the urine is an index of the excretion of urinary solids. If the latter were all heavier than water, the last two figures of the specific gravity (expressed in four figures) would directly indicate the quantity by weight of urinary solids contained in one litre of urine. As some of the excreta are, however, heavier than water, or of the same specific gravity, their weight is greater than indicated by these two figures. It has been found empirically that the last two figures of the specific gravity multiplied by 2.2337 give the weight in grains of the solids in one litre of the urine. [Example: Specific gravity = 1.018; 18 multiplied by 2.2337 = 40.2066 grains of solids in one litre of urine.] This calculation, while not absolutely accurate, is useful for comparative studies.

Pathology.—In severe *febrile diseases* the specific gravity is usually low without a corresponding increase of urine as soon as the patient's vitality begins to flag and general metabolism is reduced.

In *acute and subacute nephritis* the specific gravity is usually high, the water excretion correspondingly reduced. In the healing stage of acute nephritis the flow often increases, whereas the specific gravity remains low; this indicates that the kidneys are regaining their power to excrete water, but not as yet to eliminate solids. In acute exacerbations of *chronic nephritis* and in the terminal stages of destructive inflammation and degeneration of the kidneys the specific gravity is reduced; when it occurs suddenly, this is a bad prognostic omen, and often indicates threatening uræmia. In contracted kidney the specific gravity is low and the flow abundant. In diabetes mellitus the flow is great and the specific gravity very high, whereas in diabetes insipidus the flow is also great, but the specific gravity very low.

Determination.—The specific gravity may be determined (*a*) by weighing with a hydrostatic balance, (*b*) with a pyknometer, and (*c*) with an aerometer. The first method is useful only in very exact work, and requires a complicated balance; it will not be described here. The second and third methods are useful for clinical work. In ordinary comparative studies the aerometer is quite sufficient.

The *pyknometer* is a flask with a long neck that is drawn out in one place (see Fig. 4852); at the narrowest point is a mark; the flask is closed with a ground-glass stopper. The flask is first filled with distilled water to the mark and weighed; it is then filled with the filtered urine to the mark and weighed again. The weight of the urine divided by the weight of the water gives the specific gravity. It is very important that the temperature of the water and that of the urine should be exactly alike when the pyknometer is filled and when it is weighed. For other forms of pyknometers than the one shown in Fig. 4852, see text-books.

FIG. 4852.—Pyknometer.

The *aerometer* (urometer). This instrument consists of a glass cylinder and a float (see Fig. 4853). The latter should be graduated from 1.000 to 1.040. It is better to have two floats, the one reading from 1.000 to 1.020 and the other from 1.020 to 1.040. The urine is poured into the cylinder, the float introduced into the urine, and the specific gravity read off directly from the aerometer scale. Here, too, the temperature is important; it should be about 17.5° C., for the aerometers are graduated at this temperature. If the urine is warmer than 17.5° C., one-third of a urometer degree should be added for each degree of temperature; if the urine is colder than 17.5° C., the reading should be corrected by subtraction—one-third urometer degree for each degree of temperature. [Example: Urine 20.5° C., specific gravity 1.017. Corrected, $1.017 + 3 \times \frac{1}{3} = 1.018$.] A temperature scale is found on many urometers.

REACTION.—Normal urine is never neutral to litmus; it is either acid, amphoteric, or alkaline. The acidity is never due to the presence of free acid, but to the excess of acid salts (monobasic phosphates and urates) over alkaline salts (dibasic phosphates and urates). When the two are mixed in certain definite proportions the reaction becomes amphoteric. The urine becomes alkaline after eating (HCl—secretion) and after the ingestion of certain salts of vegetable origin (citrates, tartrates, etc.), as the latter are excreted as carbonates. Old urine is usually alkaline as the micrococcus ureæ generates ammonium carbonate.

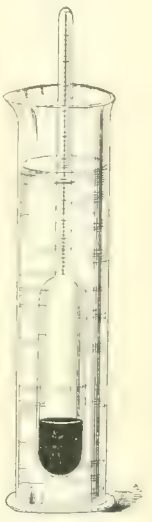


FIG. 4853.—Aerometer.

Pathologically the acidity of the urine is always increased in febrile processes, for here increased katabolism of proteid with liberation of sulphuric and phosphoric acids from proteid-sulphur and proteid-phosphorus occurs. In leukæmia, scurvy, and diabetes the urine is also in general acid.

Increased alkalinity is a valuable sign only if the above-named physiological factors can all be excluded. It is important to determine whether the urinary alkalinity is due to the liberation of ammonia or to the presence in solution of fixed alkali. Free ammonia signifies fermentation of the urine and points to cystitis. Fixed alkali appearing in excess in fresh urine may be due to the withdrawal of acid from the body (vomiting and frequent lavage), to the admixture of alkaline secretions from the urinary passages, or to the rapid absorption of exudates and transudates.

Determination.—For clinical purposes the litmus test is sufficient: blue litmus paper turning red in acid urine, and red litmus paper turning blue in alkaline urine. If the blue color remains after the paper dries, the alkalinity is due to fixed alkali; if it vanishes, to free ammonia.

Optical Properties.—(*a*) *Color.* The color of the urine is dependent on its concentration, its reaction, and the pigments it contains. Normal urine may be from pale yellow to reddish-brown. The greater the concentration the darker the color. Acid urine becomes more pale when it is alkalinized, and alkaline urine darker when it is acidified.

Certain pathologic pigments change the color of the urine. Bile pigment colors it green or brown, blood pigment red to brown red, urobilin dark brown, and melanin brown to black. Certain aromatic decomposition products that are found in the body (indican, phenols) cause the urine to turn dark on standing. Certain fruits (cherries, raspberries, etc.) and certain medicaments impart a characteristic color to the urine (see carbolic acid, coal-tar preparations, resorcin, naphthol, salol, chrysarobin, rheum, senna, santonin, etc.).

(*b*) *Fluorescence.* Pale yellow normal urine shows a bluish, yellowish-red urine, a greenish or yellow fluorescence. Urine containing albumin shows more fluorescence than normal urine, and ammoniacal urine more than urine that is not decomposed.

(*c*) *Behavior toward Polarized Light.* Normal urine is almost always slightly lævorotary; it is never dextrorotary, and hardly ever optically inactive. The presence of certain abnormal constituents (dextrose, levulose, glycuronic acid, etc.) produces typical polarimetric phenomena that will be described below.

(d) *The Spectrum.* Normal urine shows no absorption bands, but the coefficient of light extinction varies in different regions of the spectrum. In pathologic urines hæmatoporphyrin, uroerythrin, and urobilin produce typical spectra (see below).

Odor.—Fresh normal urine has a characteristic odor that is not disagreeable. The disagreeable, so-called, urinous odor is due to the presence of bacterial decomposition products (probably ammonia and phenols). Occasionally the urine emits an odor of H_2S (hydrothionuria). Certain substances impart a characteristic odor to the urine when taken by mouth (valerian, garlic, copaiba, cubebs, saffron, turpentine [violets], etc.). The peculiar odor of the urine after eating asparagus is due to methylmercaptan.

Transparency.—Normal acid urine is clear, for the normal acid and neutral salts of the urine are all readily soluble in water. Normal acid urine becomes cloudy if more quadriurate is excreted than can be dissolved in the urinary water. Normal alkaline urine is always cloudy, for the alkaline salts of the urine (*i.e.*, normal phosphates and carbonates and diphosphates of the alkaline earths) are essentially insoluble in water or in the mixture of neutral and acid salts in solution in the urine. The proteid constituents of clear urine are not in true solution, but in colloidal solution; hence the tendency of the urine to filter with decreasing rapidity. The scanty epithelia, the mucin bodies, and the crystals in suspension in normal urine form a fine cloud (nubecula) on standing.

Freezing Point (Cryoscopy).—The freezing point of the urine may be considered an index of the osmo-regulating function of the kidneys. The attempt has been made to utilize freezing-point determinations ("cryoscopy") in the diagnosis of renal diseases. The results obtained so far by different investigators are, however, ambiguous, even contradictory, so that this method is for the present of subordinate importance. This field is nevertheless promising, and as soon as the technique shall be simplified and perfected cryoscopy may become a valuable laboratory adjuvant to diagnosis. For a review of the complete literature to date see H. Strauss: *Zeitschr. f. klin. Med.*, 1902, vol. xlvii., pp. 337 to 407.

Electric Conductivity.—The resistance offered by the urine to the passage of an electric current has been utilized in order to determine the quantity of mineral salts present in the urine. There is without doubt a connection between the total ash of the urine and its conductivity. Only those urinary constituents can be estimated by determining the electrical conductivity that are electrolytes, and it might be imagined that the large number of non-electrolytes that may be present in normal and pathological urines would interfere with this determination. It has been shown, however, that such bodies as urea, uric acid, even sugar and albumin in the quantities ordinarily present in pathologic urine, exercise only a very small effect in lowering the conductivity of the urine. The conductivity of the urine is essentially, therefore, a function of the total mineral content, and the determination has a significance similar to that of the determination of the specific gravity. It is, however, more accurate. This method, when simplified as to technique, will prove a valuable aid in the determination of the eliminatory power of the kidneys for inorganic constituents. In combination with similar determinations with the blood serum it promises to throw much light on the pathology of renal insufficiency and of a variety of metabolic disorders.

CHEMICAL EXAMINATION.

Organic Constituents.

The Albumins.—*Albuminuria.—Physiological Albuminuria.* Every urine contains traces of albumin that are derived from cellular elements. This albumin is nucleo-albumin and differs from the albumins of the serum; the quantities normally present in the urine are so small that they cannot be detected by ordinary tests; the substance must first be isolated from large quantities. Every albuminuria of an *hæmatogenic* type must be considered pathological, and the conception of a *physiological* excretion of serum-albumin that some authors advocate should be discarded. All that the term physiological albuminuria implies is that a small quantity of blood albumin may occasionally be excreted in apparently healthy subjects; that this albuminuria may be transitory, and that it may lead to no serious consequences. A biologic phenomenon, however, because it is innocent, need not, therefore, be physiological. Transitory albuminuria in otherwise healthy persons (muscular exercise, cold bathing, pregnancy, and psychic shock) must always be attributed to circulatory disturbances in the kidneys or to slight nutritional impairment of the glomerular or tubular epithelia. Subjects with such albuminurias should always be considered predisposed to proper renal disease.

Pathological Albuminuria. Fluids containing albumin (pus, blood, lymph, cystic fluid, and sperma) may enter the urine below the kidneys (*albuminuria spuria extra-renalis; pseudo-albuminuria*), or soluble albumin may enter the urine within the kidneys from the blood (*albuminuria vera-renalis*). The two forms can usually be differentiated without difficulty. In *A. extra-renalis* the centrifuged and filtered urine contains only a small percentage of albumin as compared to the number of cellular elements in the sediment. If the latter consists of pure pus, the albumin percentage in the filtrate compared with the number of cellular elements in 1 $mm.^3$ of the sediment should be as 1:50,000. If it exceeds this proportion, then the albuminuria should not be considered due to the admixture of pus alone. In affections of the kidneys that produce only a slight degree of true albuminuria (contracted kidney) the combination of extra-renal albuminuria (*e.g.*, cystitis) and renal albuminuria may be difficult to recognize. Here the study of the cellular sediment, on the one hand, of general clinical symptoms (heart, arteries, and retina), and of certain peculiarities of the urine (quantity and specific gravity) on the other, must determine the diagnosis.

In *A. renalis* the excretion of albumin may be due to (1) inflammatory and degenerative lesions of the renal tissues; (2) circulatory disturbances in the kidneys; (3) certain febrile diseases (bacterial toxins and lowered blood pressure); (4) anæmia and cachexia (hæmatogenous albuminuria). Finally, there are certain forms of cyclic and intermittent albuminuria of unknown etiology occurring in healthy subjects or in sufferers from very chronic types of nephritis.

In acute nephritis the percentage of albumin is high (as high as five per cent., although usually not above one per cent.). In certain chronic forms of nephritis the percentage may be equally high. As a rule, however, the more chronic the nephritis the smaller the percentage of albumin. In very chronic forms there may even be no albumin at all.

In true albuminuria the urine may contain the following albumins alone or in combination: (1) Serum-albumin (serin); (2) serum globulin (paraglobulin); (3) mucin (nucleo-albumin); (4) albumose; (5) peptone; (6) fibrin (fibrinogen?); (7) hæmoglobin (methæmoglobin); (8) "Bence-Jones albumin"; (9) histon and nucleo-histon.

Serum Albumin and Globulin.—These two albumins almost invariably occur together in pathological urine. The proportion of the two, the so-called "albumin quotient" (serum-globulin), varies greatly in different cases. It may, moreover, differ not only from the quotient of normal serum, but also of the serum of the nephritic patient. The tests for serum-albumin and globulin may be described together.

Tests. Only those four tests are given here that are of value clinically and that render it possible to differentiate these albumins from albumoses, nucleo-albumins, etc. For the numerous other albumin reactions I refer to text-books of physiological chemistry.

1. The Nitric Acid Test.—A small quantity of cold filtered urine is poured into a test tube and a few cubic centimetres of concentrated nitric acid allowed to slowly

flow down the sides of the vessel. If albumin is present, an opaque zone forms at the plane of contact; if the amount of albumin is small, the ring may not form for one or two minutes.

Urates, certain balsams, and resins may form a similar ring; the albumin ring, however, begins at the plane of contact and extends upward, whereas the urate ring is more apt to begin above the plane of contact and gradually extend down to the acid. The urate ring, moreover, does not appear if the urine is well diluted. It also disappears on heating. The ring produced by balsams and resins is soluble in ether, and may be made to disappear by heating the liquid with this solvent. Nucleo-albumin and albumoses also form a ring with nitric acid. The test should always be repeated with diluted urine; if the ring becomes thicker in the diluted urine, the presence of nucleo-albumin is rendered probable. The albumose ring disappears on heating and reappears on cooling, the liquid meanwhile turning bright yellow; if the liquid becomes only partially clear on heating, albumin and albumoses may be present together. Urea, if present in large quantities, may crystallize out in this test as urea-nitrate and form a white zone above the acid. The crystalline character of this precipitate usually reveals its origin. If the urine contains much pigment or indoxyl multicolored rings may appear below the albumin ring.

2. The Boiling Test.—The urine is slightly acidulated with acetic acid and boiled. A flocculent precipitate may be due to the presence of albumin or of earthy phosphates. One or two drops of nitric acid for every cubic centimetre of the urine are now added; if the precipitate dissolves, it consisted of phosphates; if it does not dissolve, or if it becomes more intense, it consisted of albumin. Care must be taken to add just enough nitric acid, for, if too little is added, only a portion of the basic phosphates is converted into acid phosphates and the albumin in combination with a base (albuminate) remains in solution; if too much nitric acid is added, albumin-nitrate forms, and this, too, remains dissolved. The danger of dissolving the albumin in an excess of acid is decreased if acetic acid is used instead, and if the urine, prior to boiling, is mixed with one-sixth volume of saturated sodium chloride solution.

Bence-Jones albumin also coagulates on heating in acid urine, but at a low temperature (50° C.), and on boiling this coagulate disappears. Albumoses and nucleo-albumins (mucins) are not precipitated by this test.

3. The Potassium Ferrocyanide Test.—This is the most delicate one of the ordinary clinical tests. The urine is rendered strongly acid with acetic acid and a ten-per-cent. solution of potassium ferrocyanide, added drop by drop. If albumin is present even in traces, a cloudiness appears at once; if large quantities are present, a flocculent precipitate appears. In this test the urine should first be filtered until it is clear; if owing to the presence of microbes the urine cannot be cleared, a specimen of the urine should always be compared with the specimen treated with the reagent in order to determine whether the cloudiness has become more pronounced in the latter. It is well to dilute the urine for this test.

Albumoses are also thrown down, but they dissolve on boiling the liquid and reappear on cooling. If the urine contains much mucin or urate, precipitates form when the acetic acid is added; but they can both be made to disappear if the urine is warmed.

4. The Biuret Reaction.—The urine is treated with potassium hydrate solution and a ten-per-cent. copper sulphate solution added drop by drop. In the presence of albumin alone the liquid turns pure violet; in the presence of albumoses or peptones it turns rose; if albumin and albumoses or peptone are present together, the urine assumes tints intermediary between violet and rose. If small quantities of albumins are present, care must be exercised not to add too much copper solution, as otherwise the violet or rose tint is obscured by the blue of the reagent.

Special Test for Globulin.—The excretion of globulin is of subordinate clinical interest; only a few cases are on record in which it appeared alone in the urine; occasionally, however, it may be desirable to examine the urine for its presence. The following method is practical:

The urine is mixed with an equal volume of saturated ammonium- or magnesium-sulphate solution; this precipitates the globulins and albumoses, but leaves the serum-albumin in solution (the latter being precipitated only if the urine is saturated with the above salts). The precipitate is dissolved in one-per-cent. soda solution and the liquid acidified with acetic acid. Albumoses remain in solution while globulins are precipitated, and this precipitate, moreover, is insoluble in sodium chloride solution.

Quantitative Estimation of Coagulable Albumin.—For accurate determinations a measured quantity of the urine should be acidified and boiled, the coagulate collected in a weighed filter, washed with water, alcohol, ether, dried to a constant weight, and weighed. A nitrogen determination is then made with a portion of this residue (Kjeldahl method, see below), and the value obtained multiplied by 6.25 (albumin contains 16 per cent of N; if therefore we find X nitrogen, this corresponds to $\frac{100}{16} = 6.25$ times X of albumin). The figure obtained by this multiplication indicates in grams the amount of albumin present in the quantity of residue used for the determination. From this the amount present in the total urine can be calculated.

FIG. 4854.—Esbach's Albuminometer.

For ordinary clinical purposes of comparison the method of Esbach is sufficiently accurate. The method is based on the precipitation of albumin by picric acid. The apparatus used is called Esbach's albuminometer (Fig. 4854) The tube is filled with urine to *U* and with reagent to *R*. The two liquids are thoroughly mixed by inverting the tube several times. The apparatus is then allowed to stand for twenty-four hours at room temperature and the height of the column of precipitate determined. The figures ½ to 7 on the apparatus below *U* indicate the amount of albumin in grams per litre of urine; if, therefore, *e.g.*, the height of the column of coagulate corresponds to 3, the urine contains 3 gm. of albumin to the litre (1,000 c.c.), or 0.3 per cent. Esbach's reagent is 10 gm. of picric acid and 20 gm. of citric acid dissolved in 1 litre of water. In this test the reaction of the urine should be acid, its specific gravity not above 1.010, and it should not contain more than 0.4 per cent. of albumin; otherwise the determination is not accurate. It will be necessary, therefore, as a rule, to dilute and acidify the urine prior to making the determination. Occasionally the precipitate of albumin will not settle; then this method cannot be employed; nor can it be employed if the urine contains quinine or antipyrin.

Nucleo-Albumin (Mucins).—The mucin of the older writers has been shown to consist of albumin in combination with one of these acids that are usually present in the urine, viz., nucleinic acid, chondroitin-sulphuric acid, and taurocholic acid. On the addition of acetic acid to the urine these compounds are precipitated as nucleo-albumin, chondro-albumin, and albumin taurocholate. These bodies alone or combined form "mucin," and it is quite clear that the character of this substance must vary according to the relative quantities of these acids present in the urine. The taurocholate is often absent from normal urine, but it is present in abundance in icteric urine. Chondro-albumin is a glycoproteid and can be split into proteid and carbohydrate, while nucleo-albumin is a "phosphorous proteid" and can be split into proteid and nuclein.

Mucins are always present in traces in normal urine. They are excreted in excess in desquamative catarrh of

the urinary passages, in infectious forms of nephritis (diphtheria and scarlatina), in toxic nephritis (tar, pyrogallol, corrosive sublimate, arsenic), in typhoid fever, in croupous pneumonia (disappearing within twenty-four to forty-eight hours after the crisis), after chloroform anæsthesia, and, particularly, in icterus.

Tests. Clouding of the diluted urine with acetic acid speaks for the presence of mucin bodies; if the mixture is shaken with chloroform or ether, a cloudy ring of mucin forms at the plane of contact after the liquids have been allowed to separate. Mucins give the nitric acid test (see above), but the ring of coagulate first forms 0.5 to 1 cm. above the acid and later extends down to it. If the urine is sufficiently diluted, the urate ring, that behaves similarly, is not formed. In order fully to identify the substance it must be isolated from large quantities of the urine (see text-books of physiological chemistry).

Albumoses and Peptone.—It is doubtful whether peptone (in the sense of Kühne) ever appears in the urine. Recent investigations have shown the peptones of the older writers to be albumoses (hemialbumose, deuteroalbumose [peptone in the sense of Brücke], propeptone, histon, etc.). All these bodies appear in the urine when the intracellular disassimilation of the proteids is perverted as the result either of bacterial invasion (suppuration, tuberculosis), or of intoxication with certain inorganic poisons (phosphorus), or of certain metabolic disorders of unknown pathogenesis (osteomalacia). Pyogenic "peptonuria" is clinically important, for the diagnosis of "pus somewhere" may frequently be strengthened by the appearance of albumoses in the urine; the differentiation is also occasionally possible, with the aid of this sign, between purulent and tuberculous or simple serous exudates (meningitis, pleuritis, etc.).

Tests. In order to get rid of the common albumins the urine is treated with an equal volume of saturated salt solution, acidified with acetic acid and boiled. The solution is filtered hot; coagulated albumins remain behind while albumoses go into the filtrate from which they separate on cooling. The filtrate should give the biuret reaction (see above), and the precipitate formed on cooling should redissolve on boiling.

The differentiation of the different albumoses that may be present in the urine is possible, but the chemical manipulations incident to this separation are so complicated that a description of these methods lies beyond the scope of this article. (For an excellent exposé of the subject see Neubauer u. Vogel, "Harnanalyse," 1898, pp. 466 to 484.)

Fibrin (*Fibrinogen*).—These bodies occasionally appear in the urine in chyluria and in hæmaturia, also in croupous inflammation of the urinary passages (tuberculosis, diphtheria). Fibrinogen only appears in profuse hæmaturia, and its presence may be suspected from the formation of coagula in the urine; the latter may form either within the urinary passages or not until the urine is voided.

Test. The coagula are filtered off, repeatedly washed with a five- to ten-per-cent. solution of NaCl dissolved in a boiling one-per-cent. soda solution, or in a 0.5-per-cent HCl solution (the coagulate must not dissolve in *cold* soda or HCl solution!), and the liquid submitted to the ordinary tests for albumin. If the coagula consisted of fibrin, these tests will be positive.

Hæmoglobin (*Methæmoglobin*)—*Hæmaturia, Hæmoglobinuria.* In *hæmaturia* the blood enters the urine somewhere in the urinary passages; it may be the result of acute inflammatory affections, neoplasms, or trauma of the kidneys, ureters, bladder, or urethra.

In *hæmoglobinuria* blood pigment that is already in solution in the renal blood passes through the renal epithelia into the urine; hæmoglobinuria may be the result of poisoning (potassium chlorate, mushrooms, sulphuretted hydrogen, arseniated hydrogen, pyrogallic acid, etc.); it may also follow the transfusion of blood from one species to another; it may follow severe cutaneous burns and certain infectious diseases. Finally, there is an independent form of paroxysmal hæmoglobinuria of unknown etiology.

In hæmoglobinuria the filtered urine is always red, whereas in hæmaturia, provided the urine is fresh, the filtrate may be colorless. Other substances than blood pigment may, however, impart a red color to the urine so that recourse must be had to one of the following tests in order to establish the presence of hæmoglobin in the urine. (For the detection of blood corpuscles in the sediment see below.)

Tests. 1. Boiling.—In the presence of blood pigment a brown coagulate forms that usually floats on the surface of the liquid and that can be decolorized by shaking the urine with sulphuric acid-alcohol.

2. Heller's Test.—This test is based on the formation of hæmochromogen from hæmoglobin by the action of caustic alkali. Five drops of a ten-per-cent. sodium hydrate solution are added to half a test tube of urine. The mixture is boiled and allowed to stand. The earthy phosphates and carbonates in the precipitate will be found colored brown, brown-red, or blood-red (hæmochromogen spectrum). In alkaline urine the test may fail because the phosphates are already precipitated; to such urine an equal volume of normal acid urine may be added in order to obtain the reaction.

3. Almén's Test.—To 10 c.c. of urine is added a mixture of 5 c.c. of *old* oil of turpentine, and 5 c.c. of tincture of guaiac. If blood pigment is present, a white ring will form that gradually turns blue. The test may be modified by adding 5 c.c. of ether and shaking the mixture; the ether dissolves the pigment and forms a blue layer on top of the urine.

4. Teichmann's Test.—The precipitate obtained in tests 1 or 2, or, better still, the precipitate obtained by the addition to the urine of tannin solution, is filtered off, washed with water and allowed to dry in the air. A small portion is placed on a slide with a crystal of sodium chloride and a drop of glacial acetic acid, covered with a cover slip and heated to boiling for about one minute, the evaporating fluid being constantly replaced by glacial acetic acid, drop by drop. As soon as the fluid turns brown, it is allowed to cool slowly. Under the microscope *hæmin* crystals (Teichmann's crystals, Fig. 4855) of characteristic form and arrangement will be seen.

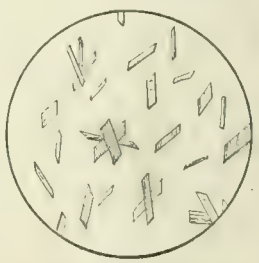


FIG. 4855.—Teichmann's Crystals.

5. Spectroscopic Test.—The diluted urine on direct spectroscopic examination gives the spectrum either of oxyhæmoglobin or of methæmoglobin, provided the urine is acid. On addition of ammonium sulphide the spectrum of gas-free, reduced hæmoglobin appears. After treating the urine with caustic alkali (see Test 2) the spectrum of hæmochromogen appears.

"*Bence-Jones Albumin.*"—This body occurs in the urine in association with multiple myomata of the bones. Nothing is known of its origin. It may be formed in the intestinal tract by some perverted process of disassimilation. This albumin is usually considered an albumose, but it differs from all other known digestive albumoses. It, moreover, resembles true albumin inasmuch as it coagulates on heating to 100° C. (Magnus-Levy), and yields primary and secondary albumoses on peptic digestion. No hetero group can, however, be demonstrated among the digestive products. The body has been found crystallized in the urine.

Test. If urine gives a marked albumose reaction (see above), the presence of Bence-Jones albumin may be suspected, for only in "Bence-Jones albumosuria" do we find such large quantities of "albumose." Such urine should be treated with an equal volume of saturated ammonium-sulphate solution—in this way the body is salted out. It can be further identified by submitting it

to peptic digestion and determining the absence of hetero-albumose and the presence of proto-albumose in the mixture of digestive products.

Histon and Nucleo-Histon.—These two albumins are derived from the cell nuclei; they occasionally appear in the urine in affections accompanied by great destruction of leucocytes.

Test. The urine is freed from albumin by boiling, cooled, and precipitated with four volumes of alcohol (95 per cent.). The precipitate is dissolved in hot water and the solution allowed to cool. In order to get rid of uric acid it is acidified with HCl and allowed to stand for four hours; the uric-acid crystals are filtered off and the filtrate precipitated with ammonia; the precipitate is then washed with water containing a little ammonia and redissolved in diluted acetic acid. This solution, if histon is present, should coagulate on boiling and give the biuret reaction.

NITROGENOUS CONSTITUENTS OTHER THAN ALBUMINS.—From eighty-three to ninety-three per cent. of the urinary nitrogen is secreted as urea; the remaining seven to seventeen per cent. of nitrogen appears in the urine in the form of diamins, amido acids, urea, purin bodies (uric acid and its congeners), nucleinic acid, creatin and creatinin, oxaluric acid, allantoin, preformed ammonia, etc.

The Total Nitrogen and Nitrogenous Equilibrium.—We speak of nitrogenous equilibrium when the output of nitrogen corresponds to the intake. The level of nitrogenous equilibrium varies in different persons and in one and the same individual at different times. It is dependent on the health of the subject, the mode of life, the composition of the food, etc. The following rules govern the level of nitrogenous equilibrium: If an individual is fed on a constant diet sufficiently abundant to maintain full nutrition, then the urinary N-excretion becomes constant at the expiration of from two to four days. The organism, however, has a tendency to accommodate the N-output to the N-intake; and the N-output of one period of twenty-four hours is dependent on the N-intake of the preceding period of twenty-four hours. If the N-intake is altered, the latter factor chiefly determines the N-output in the beginning; after the expiration of a number of days, however, the determining influence of the former factor predominates. If, therefore, the N-intake fluctuates from day to day, the sum of the N-output during a prolonged period of time will equal the sum of the N-intake during this time; but for individual periods of twenty-four hours during this time great differences in the N-output will become apparent. It is clear, therefore, that any calculation in regard to the relation between N-intake and N-output that is based on an observation extending only over a period of twenty-four hours is altogether devoid of value.

A healthy adult can maintain N-equilibrium on 0.6 gm. of albumin per kilogram body weight pro die—or with more. As soon as less N is ingested, N-equilibrium can no longer be maintained, for the organism then begins to disassimilate its proper tissues in order to cover the deficit. The *upper* boundary of N-disassimilation has so far not been determined.

Determination of Total Urinary Nitrogen.—Considerable N is eliminated in the fæces; this N is in part derived from the gastro-intestinal secretions, in part from desquamating epithelia, and in part from ingesta that are not absorbed. This amount of N must be included in the calculation, and must be determined in metabolic studies. N-equilibrium is only established when Food-N *minus* Fæces-N *equals* Urine-N.

The urine should be gathered from morning (before breakfast) to the following morning, not from night to night. The N found in such urine correctly indicates the total N excreted in twenty-four hours: (*a*) if the last nitrogenous food is ingested at least eight or ten hours prior to the collection of the last urine (hence the advantage of collecting from morning to morning); (*b*) if no great fluctuations are permitted in the amount of water ingested during the period of observation as against previous periods; for abundant water-drinking washes out an abnormal amount of nitrogenous material, whereas restriction of fluids exercises the reverse effect and favors the retention of nitrogenous material.

The Kjeldahl Method for Determining the Urinary N.—This method is simpler than all other methods for determining nitrogen; it is more rapid and does not require so much skill and experience on the part of the operator. The method is based on the following principle: The nitrogenous substances of the urine on boiling with concentrated sulphuric acid are destroyed and all the nitrogen that is not in direct combination with oxygen is converted into ammonia, and hence is present in the solution as ammonium sulphate. If the acid solution is now treated with hot soda lye, the ammonia is liberated; it is distilled into a measured quantity of normal acid and the excess of acid titrated back.

According to the concentration of the urine 5 c.c. or 10 c.c. of urine are poured into a so-called Kjeldahl flask (*i.e.*, a flask of hard glass with a round bottom and a long neck, holding from 200 to 300 c.c.); to this are added 20 c.c. of concentrated H_2SO_4, and a small quantity (about one-third gram) of the yellow oxide of mercury. The mixture is boiled until the solution becomes quite colorless, care being taken not to heat too rapidly in order to prevent the escape of vapors. On cooling, the contents of the Kjeldahl flask is transferred to a Kjeldahl retort by repeated rinsing with a little distilled water. The Kjeldahl retort is a large round-bottomed flask holding about 500 c.c. To the liquid in this retort are added 40 c.c., of a solution of sodium sulphide (40 gm. to 1,000 c.c. of water), 160 c.c. of sodium hydrate solution (270 gm. to 1.000 c.c. of water), and a small quantity of talcum. The sulphide is necessary in order to decompose the amido-compounds of mercury that form and that would not give up all their nitrogen if sodium hydrate alone were used. The talcum is added in order to render ebullition more gentle and to prevent bumping. As soon as all the solutions have been poured into the retort it is immediately connected with a condenser and the distillation begun. The vapors of ammonia and the water are collected in a flask containing 40 c.c. of a one-fourth normal H_2SO_4; the distillation is continued until about two-thirds of the fluid have gone over; the condenser is then rinsed with water and the washings added to the distillate. The acid is now retitrated with a one-fourth normal sodium hydrate solution, using rosolic acid as an indicator. The difference indicates the amount of acid neutralized by the ammonia. As 1 c.c. of the one-fourth normal solution represents 0.0035 gm. of N, this figure must be multiplied by the number of cubic centimetres of urine (5 or 10) used for the analysis in order to determine the amount of N contained in this quantity of urine. The N in the twenty-four hours' urine can easily be calculated from this. There are numerous modifications of the Kjeldahl method, but the above plan has been found quite satisfactory and altogether reliable in the hands of the author. (For these modifications and for certain refinements of the methods I refer to Huppert: "Analyse des Harns," 1898, pp. 801 to 807).

Diamins.—The diamins (putrescin and cadaverin) are of rare occurrence in the urine of man and are of subordinate clinical importance.

Amido Acids.—Of this group of nitrogenous urine bodies *carbamic acid* is occasionally found in normal urine, but it has no clinical significance. It is too rare, moreover, to merit discussion in this condensed article. Other members of this group—viz., cystin, leucin, and tyrosin—frequently appear in the urine in crystallized form; they will hence be discussed in detail under the heading of urinary sediments (see below).

Urea.—The excretion of urea is dependent on two factors, viz.: (1) the ingestion of nitrogenous food (chiefly albumins); (2) the catabolism of the organized albumin of the body. As the latter factor is a minor source of urea, and as it is, moreover, fairly constant, the excretion of urea may be said to be largely dependent on the inges-

tion of proteid pabulum. In interpreting the plus or minus of urea excretion both factors must nevertheless be included in the calculation, for it is clear that a diseased person who is consuming an abnormal quantity of the organized albumin of his proper tissues, and at the same time is eating a normal amount of proteid food, will excrete more urea than a healthy individual who is destroying a normal amount of body tissues and is eating the same amount of food. Or, again, a healthy, underfed subject will excrete less urea than an underfed, diseased subject, for the latter contributes more to the urinary nitrogen from his own tissues.

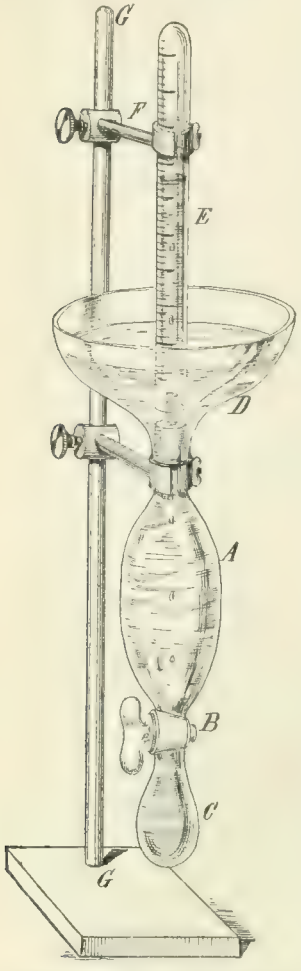


FIG. 4856.—Hüfner's Apparatus.

Normal urine contains as much as four per cent. of urea. The average quantity excreted in twenty-four hours by a healthy adult on a mixed diet is 33 gm. Fluctuations in the urea excretions from 20 to 45 gm. may nevertheless still be within physiological limits; a person performing hard physical labor will excrete more than 33 gm.; a person leading a sedentary life less. On a diet containing little N or after fasting the urea excretion may fall to 15 to 20 gm. Women excrete from 20 to 32 gm. a day. On a diet rich in N as much as 100 gm. may be excreted. The excretion of urea is always increased in febrile diseases, and in diabetes mellitus. It is always decreased in affections of the liver and kidney parenchyma, and in all chronic disorders that are accompanied by malnutrition.

Tests. Qualitative tests for urea are of no clinical importance. Quantitative estimations of the urea excretion, on the other hand, are of great clinical interest as an index of a variety of functional and organic perversions that have been indicated above.

Estimation of the Urea from the Specific Gravity of the Urine.—As urea is the chief solid constituent of the urine, the urea content can be approximately estimated from the specific gravity. Empirically it has been determined that urine of a specific gravity of 1.014 contains about one per cent. of urea; of 1.014 to 1.020, about one and a half per cent.; of 1.020 to 1.024, about two to two and a half per cent.; of 1.028, about three per cent. of urea. In febrile and cachectic states, in which the urinary chlorides are reduced, this estimation must be corrected. For the chlorides in these diseases are excreted in such small amounts that they exercise no appreciable influence on the urinary specific gravity. Consequently, a given specific gravity indicates *more* urea than is given in the above figures.

Of the accurate methods for determining urea the method of Hüfner is the most convenient for clinical work, the method of Mörner and Sjöquist the most accurate for scientific work. These two methods alone will therefore be described. The titration method of Liebig-Pflüger, the method of Folin, etc., are all very good, but they do not surpass in convenience nor in accuracy the two methods mentioned and to be presently described.

The Hypobromite Method of Hüfner (Knop).—This method is based on the fact that sodium hypobromite in alkaline solution decomposes urea into nitrogen, carbon dioxide and water, according to the following formula:

$$\underset{\text{Urea.}}{CO(NH_2)_2} + \underset{\text{Sodium hypobromite.}}{3NaOBr} = 3NaBr + CO_2 + 2H_2O + 2N$$

The CO_2 that develops is absorbed by the soda lye while the N passes through the lye and is measured; from the volume of N liberated the amount of urea can be calculated. This method is inaccurate in two respects: (1) the amount of N liberated is never quite as large as the theoretical amount; (2) hypobromite of soda also liberates N from other nitrogenous constituents of the urine than urea. Notwithstanding these two sources of error, the method is sufficiently accurate to merit general employment.

Hüfner's Apparatus (Fig. 4856) consists of three parts, viz.: (1) a cylindrical vessel, *A*, connected by a glass cock, *B*, with a smaller cylindrical receptacle, *C*; (2) a dish, *D*, that is connected with the upper end of *A* by a rubber cork (as shown in the figure), so that the open upper extremity of *A* protrudes into *D*; (3) an eudiometer tube, *E*, that should be from 30 to 40 cm. long, 2 cm. wide, and should be graduated for 0.2 cm. The eudiometer tube can be held in an inverted position over the upper end of *A* by a clamp, *F*, attached to a stand, *G*.

The Hypobromite Solution.—Seventy cubic centimetres of thirty-per-cent. sodium hydrate solution are diluted with 180 cc. of distilled water; the solution is then mixed with 5 c.c. of bromine. The bromine dissolves in the lye, and sodium bromide and sodium hypobromite are formed according to the formula:

$$3NaOH + Br_2 = NaBr + NaBrO + H_2O$$

The hypobromite solution should be kept in a cool, dark place in a tightly stoppered bottle, and should be made fresh every few days, as otherwise the sodium hypobromite is apt to decompose into sodium bromide.

Method of Performing the Determination.—The urea content of the urine is first estimated from the specific gravity (see above) and the urine diluted so as not to contain more than one per cent. of urea. Of this diluted urine exactly 5 c.c. are allowed to flow from a long pipette into the small receptacle, *C*, care being taken not to spill any of the urine in *A*, the pipette is carefully rinsed with water, and these washings also allowed to flow into *C*, until the latter receptacle is filled to the cock, *B*. The cock is now closed. *A* is now filled to overflowing with hypobromite solution; the dish, *D*, and the eudiometer tube, *E*, are then filled with concentrated NaCl solution and the latter inverted in the former and held over the open upper end of *A* by the clamp, *F*. The cock, *B*, is now opened. As the hypobromite solution is heavier than the urine, it runs down through *B* into *C* and at once causes an active development of gas (CO_2 and N). The CO_2 is absorbed in the sodium hydrate solution contained in *A*, while the N rises up through *A* and collects in the tube *E*. The reaction is over in about twenty minutes. The eudiometer is then transferred to a deep vessel filled with water of room temperature and allowed to stand there for fifteen minutes; the reading is finally made in such a way that the levels of the fluid in the vessel and in the tube are made equal. At the same time the temperature of the water and the barometric pressure are noted.

The volume of gas must now be reduced to 0° C., 760 mm. and absolute dryness; this is done according to the formula:

$$V' = \frac{V\,(B - W)}{760\,(1 + 0.0036\,t)\;354.3}$$

V′ = Volumes of nitrogen (corrected).

V = Volume indicated on eudiometer.
B = Barometric pressure.
W * = Tension of water vapors at temperature t
t = Temperature of water.
0.0036 = Coefficient of expansion of gases for 1° C.

As urea only yields 354.3 c.c. of N instead of the theoretic amount of 372.7 c.c., when it is disassociated with hypobromite solution, V' must be divided by 354.3 in order to obtain the correct amount of N developed, for

$$354.3 : 1 :: V : x$$

$$x = \frac{V}{354.3}$$

If 5 c.c. of urine were employed for the determination, V' multiplied by 20 gives the percentage of urea.

A simpler apparatus, called a ureometer, has been constructed on a similar principle as Hüfner's apparatus, but the results obtained with this modified apparatus are altogether inaccurate and essentially valueless. These ureometers are unfortunately in common use.

Method of Marcet and Squirel.—The method is based on the following principle: If the urine is treated with barium chloride and barium hydrate in certain proportions, all nitrogenous constituents, with the exception of urea, are precipitated from the solution by a mixture of ether alcohol. In the filtrate the N is determined after Kjeldahl and the urea calculated from this amount of N.

Execution: Five cubic centimetres of urine (if necessary after removal of any albumin that it may contain) are treated in a small flask with 5 c.c. of baryta mixture (saturated solution of barium chloride plus five per cent. barium hydrate) and 100 c.c. of a mixture of one volume of ether and two volumes of alcohol (97 per cent.). The flask is allowed to stand for twenty-four hours; the precipitate is then filtered off, repeatedly washed with ether-alcohol; the filtrate treated with magnesia usta in order to drive off any ammonia that may be in solution, and the ether-alcohol driven off at a temperature of 55° C. The temperature should never be allowed to rise above 60° C. When the volume of the filtrate is reduced to 10 or 15 c.c, the N determination is made with a measured proportion of the liquid. The urea is calculated from the N by multiplying the latter with $\frac{15}{7}$, or 2.143.

Purin Bodies, Uric Acid and Its Congeners.—Uric Acid. Uric acid is a normal constituent of the urine. A healthy adult excretes from 0.2 to 1.25 gm. of uric acid in the twenty-four hours to from 30 to 35 gm. of urea, *i.e.*, about one to two per cent. of the urinary N appears in the urine in the form of uric acid.

The excretion of uric acid is subject to many fluctuations in health and in disease. The chief and probably the only source of uric acid are the nucleins of cell nuclei, and as these nucleins may be derived either from the food or from the cells of the tissues of the organism, the excretion of uric acid is determined on the one hand by the amount of nuclein-containing food that is ingested and on the other hand by the catabolism of the proper tissues of the body. The old view that uric acid is an oxidation product of *any* form of albumin has been shown to be wrong. The administration of very large quantities of albuminous pabulum *containing no nucleins* is not followed by an increase in the uric-acid excretion. The administration, however, of nuclein or of nuclein-containing food is always followed by increased excretion of uric acid. On the other hand, a subject fed for a long time on a diet containing no nucleins, or a subject after a prolonged period of fasting, still excretes appreciable quantities of uric acid; in the former case the increase of uric acid was derived from the food nucleins ("exogenous uric acid"); in the latter case the excreted uric acid was derived from the tissue nucleins ("endogenous uric acid"). Whereas the former factor is constant and independent of the individual in the sense, namely, that a definite quantity of food nuclein leads to the excretion of a definite and calculable quantity of uric acid, the latter factor is inconstant, varies in different individuals, and cannot be calculated in advance. It varies from 0.1 to 0.2 gm. a day in normal adults.

All attempts to find "normal" values or to determine the significance of fluctuations in the uric-acid excretion are altogether fictitious as long as the purin bodies of the food are not included in the calculation. The diversity of opinions among different authors in regard to the effect of albuminous food on the uric-acid excretion can be explained as follows: Those who argue that an albuminous diet increases the urinary uric acid experimented with a diet containing much meat (and consequently xanthin bases, nucleins, etc.), whereas those who claim that a proteid diet exercises no effect on the uric-acid excretion worked with vegetable albumins, milk, eggs, etc., all articles that contain little purin.

Pathologically the excretion of uric acid is increased in febrile disorders and in other diseases in which there is loss of tissue albumin; here the uric-acid increase usually proceeds *pari passu* with the urea increase. In leukæmia the uric acid is often absolutely increased; here the catabolism of many leucocytes must be made responsible. In gout and the uric-acid diathesis (goutiness) there is much divergence of opinion. The consensus of newer writers who looked to a constant diet of known nuclein content during their investigations seems to be that the uric-acid excretion is somewhat increased *during* the attack, and that immediately *preceding* the attack the uric-acid excretion is slightly decreased. In the intervals between the attacks the uric-acid excretion in gouty subjects differs in no way from that in normal subjects.

Qualitative Tests for Uric Acid.—See under urinary sediments (below).

Quantitative Estimation.—Of the many methods for determining the uric acid in the urine the method of Ludwig-Salkowski is the best, the most accurate, and the most rapid.

The method of Heintz was in universal use for many years. It is so simple that even to-day many clinicians employ it. While the results of this method are very inaccurate in the sense, namely, that far too little uric acid is indicated, it nevertheless has a place in the clinical laboratory for determinations of a *relative* increase or decrease of uric acid in the same individual. The method is carried out as follows: Two hundred cubic centimetres of urine are treated with 10 c.c. of concentrated hydrochloric acid; the mixture is allowed to stand for forty-eight hours and the crystalline deposit of uric acid filtered off; the crystals are washed with alcohol and ether and dried at 110° C.

The Method of Ludwig-Salkowski.—Uric acid is precipitated from urine that has been treated with an ammoniacal magnesia solution by ammoniacal silver nitrate solution. The resulting precipitate consists of silver-magnesium urate. (The chlorides remain in solution.) If this precipitate is treated with alkali sulphide, the silver is precipitated as silver sulphide, whereas the urate goes into solution as alkali-urate. From the latter solution uric acid crystallizes after acidulation and evaporation to a small volume. The crystals are gathered on a filter, washed and weighed as above. The addition of ammoniacal magnesia solution causes precipitation of triple phosphate, and this mingling with the gelatinous urate precipitate renders the latter more flocculent and easier to wash, etc.

Execution: Three solutions are required, viz.:

1. An ammoniacal silver solution. Twenty-six grams of silver nitrate are dissolved in water and so much ammonia added until the brown precipitate that forms is redissolved in the excess of ammonia. The solution is then filled up to 1,000 c.c. with water and kept in a dark place.

2. Magnesia mixture. One hundred grains of crystal-

* The values for W at ordinary temperatures are the following:

10° C. = 9,126	16° C. = 13,519	22° C. = 19,675
11° C. = 9,751	17° C. = 14,009	23° C. = 20,969
12° C. = 10,421	18° C. = 15,351	24° C. = 22,211
13° C. = 11,130	19° C. = 16,345	25° C. = 23,582
14° C. = 11,882	20° C. = 17,396	
15° C. = 12,667	21° C. = 18,505	

lized magnesium chloride are dissolved in water and a large excess of ammonia added. This leads to the precipitation of magnesium hydroxide. A solution of ammonium chloride that is saturated in the cold is now added in such quantity that the precipitate of magnesium hydroxide is redissolved. The moderately clear solution is filled up to 1,000 c.c.

3. Solution of sodium (or potassium) monosulphide. Ten grams of NaOH or 15 gm. of KOH are dissolved in 1,000 c.c. of water. One-half of this solution is saturated with hydrogen disulphide gas and then added to the other half. The KOH or NaOH employed for this preparation must be free from nitrate or nitrite, for this solution is added to the urate solution before it is acidulated; on acidulation any nitric or nitrous acid would be liberated and these acids decompose uric acid.

The concentration of these reagents is arranged so that 10 c.c. of each suffice for 100 c.c. of urine. It has been established that this proportion precipitates all the phosphates and urates, and, on the other hand, redissolves all the uric acid from the precipitates that form even if the urine contains a very large proportion of uric acid.

One hundred cubic centimetres of urine are poured into a beaker. Ten cubic centimetres of solution 1 and 10 c.c. of solution 2 are mixed in another vessel and treated with so much ammonia that the precipitate of silver chloride that forms is redissolved; sometimes a flocculent precipitate of magnesium hydroxide forms, but this does not interfere with the reaction. The reagent is slowly poured into the urine. A gelatinous precipitate forms that is allowed to settle partially and is then filtered off and washed with very weak ammonia water until the washings are free from silver and from chlorides. The precipitate is then brought from the filter into a beaker, either by perforating the filter and squirting the precipitate through, or, if a suction pump is used, by transferring the bulk mechanically with a glass rod and then rinsing the balance into the beaker with the stream from a wash bottle. Ten cubic centimetres of solution 3 are now mixed with 10 c.c. of water and heated to boiling. The filter is rinsed with this solution and the whole added to the suspension of the precipitate; the mixture is then heated to boiling over a small flame, the deposit of silver sulphide filtered off, frequently washed with hot water, washings and filtrate acidulated with dilute HCl (5 c.c. of HCl [1.12 specific gravity] diluted one-fourth are sufficient), and evaporated to about 20 c.c. On cooling, the uric acid crystallizes out. Some writers claim that all the uric acid is deposited after an hour; it is better to allow the solution to stand for at least six hours. The uric acid is filtered off, washed with alcohol and ether and weighed. For every 10 c.c. of the mother liquor and washings 0.00005 gm. of uric acid is added to the result, for this small amount of uric acid is soluble in 10 c.c. of water and consequently remains in solution.

Salkowski has modified this method slightly. Instead of decomposing the silver urate precipitate with alkali sulphide, he passes a stream of hydrogen sulphide gas through the suspension of silver urate in acidulated water; the silver salt is decomposed in the same way, the sulphide of silver being thrown down, while the uric acid passes into solution; the mixture is heated to boiling, filtered, and the filtrate treated as above. This modification has no advantages over the original Ludwig method—in fact, requires more care and more paraphernalia.

If sugar or albumin is present in the urine, they must be removed before the uric-acid determination is made. Ludwig advises removing the albumin as follows: The urine is treated with concentrated sodium chloride solution (10 to 15 c.c. to every 100 c.c. of urine), acidulated with acetic acid and boiled. The albumins coagulate and can be removed by filtration; the filtrate must be filled up to the original volume of the urine.

If the urine contains uric-acid crystals, these must be dissolved by warming before the urine is measured off. The precipitation of urates may often be prevented by adding a pinch of sodium bicarbonate to the urine immediately after it is voided.

Of other methods for determining uric acid only the underlying principles will be given in this place; for details I refer to the text-books.

Method of Hopkins. Thirty grams of ammonium chloride are dissolved in 100 c.c. of the cold urine. This leads to the precipitation of ammonium urate; the latter is filtered off and washed, then dissolved in boiling water and acidulated with HCl; after concentration of the solution and cooling the uric acid crystallizes out and can be weighed as above.

Some authors prefer to determine the amount of uric acid by *titration*, either acid metrically or with permanganate of potassium, or as silver magnesium salts (see Huppert, "Harnanalyse," 1898, p. 814).

Method of Folin. The uric acid is precipitated with the following reagent: 500 gm. of ammonium sulphate, 5 gm. of uranium acetate, 60 c.c. of a ten-per-cent. solution of acetic acid dissolved in 650 c.c. of water; 75 c.c. of this reagent are added to 300 c.c. of urine. Soon a mucoid body separates from the urine that is removed by filtration; the filtrate is then treated with concentrated ammonia; this leads to the precipitation of ammonium urate. The latter is washed into a beaker, treated with concentrated sulphuric acid, and titrated at once with one-twentieth decinormal solution of potassium permanganate. Each cubic centimetre of the reagent corresponds to 0.00375 gm. of uric acid. As ammonium urate is slightly soluble a correction of 0.003 gm. must be made for every 100 c.c. of urine.

Purin Bases. (Synonyms: Xanthin Bases, Nuclein Bases, Alloxuric Bases). To this group belong many substances, of which the following have been found in human urine: Xanthin, heteroxanthin, paraxanthin, guanin, hypoxanthin, adenin, episarcin, carnin, epiguanin, and "the unknown basis of Krüger and Wulff." The most important of these bodies is xanthin. The quantity of purin bases occurring in the urine is very small. On a mixed diet the urine voided in twenty-four hours contains 87 gm., on an animal diet 44 mgm., and on a vegetable diet (peas and cabbage) 72 mgm., or (apples and carrots) 111 mgm. If the uric-acid nitrogen voided on these different varieties of diet is calculated at 100, the nitrogen of the purin bases (figured for xanthin) equals 18.1, 7.6, 18.1, and 35.8. The amount of xanthin bases excreted, therefore, equals only a fraction of the uric acid excreted. The daily normal excretion equals from 0.015 to 0.06 gm. Of this amount 0.015 to 0.03 is xanthin; hypoxanthin and guanin are next in importance, then come paraxanthin and heteroxanthin. The other members of the group are of rare occurrence and of very subordinate importance.

The purin bases are derived from nuclein; they may consequently, like uric acid, be derived from the food nucleins or from the tissue nucleins. Their relation to uric acid is as follows: If nuclein or nuclein-containing organs (spleen pulp) are allowed to stand at body temperature with free access of oxygen, uric acid is formed; if oxygen is withheld, the purin bases are formed instead. It is possible to convert purin bases into uric acid by the aid of organ extracts, for the latter apparently contain an "oxydase" that can produce this oxidation. Pathogenetically the purin bases probably play a rôle in the uric-acid diathesis, for, as I have shown, they can cause certain renal lesions that are identical with the lesions of granular nephritis in gout, and also certain cardiovascular changes that are similar to those seen in nephritis, arteriosclerosis, etc. Much has been written in regard to the relation existing between the elimination of uric acid and of the xanthin bases. It was believed for a time that a decrease of the uric-acid excretion was compensated by a corresponding increase in the purin-base excretion in gout and gouttiness. These findings, including my own, have since, however, been shown to be uncertain, owing to the fact that the method for the determination of purin bases (Krüger and Wulff) was deficient. Both uric acid and purin bases may, of course, also be increased or de-

creased together. In leukæmia the greatest amount of purin bases and of uric acid is excreted. Tea and coffee, owing to the theobromine (dimethyl xanthin) and caffeine (trimethyl xanthin) they incorporate, lead to the excretion of methylated xanthin and heteroxanthin. Xanthin sometimes forms a crystalline sediment in the urine. This will be described under urinary sediments.

For the present the quantitative determination of the purin-base excretion is of subordinate clinical importance; the method, moreover, is complicated and requires more skill and more apparatus than are usually at the disposal of the clinician and practitioner. The following *method of Salkowski* gives accurate results. The method is based on the precipitation of uric acid and purin bases together as silver salts and the subsequent separation of the latter from this precipitate.

Execution: A measured quantity of urine is treated with ammoniacal magnesia mixture and ammoniacal silver solution, as described above (Ludwig-Salkowski method) under "uric acid." The uric acid is removed as in the Ludwig method, and the final filtrate, which contains the purin bases, together with the washings, treated with ammoniacal silver solution. This reprecipitates the purin bases. The precipitate is collected on a filter, washed, dried, incinerated. The ash is dissolved in dilute nitric acid and the silver estimated in this solution by titration. The best method of titration is with potassium sulphocyanide, using ammonio-ferric alum as an indicator. In a compound of the silver salts of xanthin, hypoxanthin, etc., one atom of silver represents 0.277 gm. of nitrogen, or 0.7381 gm. of the bases. Consequently 1 c.c. of the sulphocyanide solution will correspond to 0.002 gm. of nitrogen, or 0.00542 gm. of the bases. The sulphocyanide solution is made up as follows: The solution should contain 12.9849 gm. to a litre. The salt is very hygroscopic, so that it cannot be weighed accurately. Therefore a concentrated solution is made and standardized against a silver solution containing 29.042 of silver nitrate to the litre, using ammonio-ferric alum as an indicator.

The separation and identification of the different members of the group of purin bases is possible, but it requires very much time and considerable chemical skill. As this separation is of no clinical value, but merely of physiological interest, it will not be described in this article.

Nucleinic Acid.—This body occurs in small quantities in the urine either in combination with a proteid molecule (see nucleo-albumin), or occasionally free. Nucleinic acids are a combination of purin bases, phosphoric acid, and of a nitrogen-free molecule (possibly pentose). They contain as much as 9.5 per cent. of phosphorus; nucleo-albumins contain about 1.5 per cent. of phosphorus. Nucleinic acid is precipitated from the urine together with chondroitin sulphuric and taurocholic acids (icterus) if the greater portion of the inorganic salts are removed from the urine; the latter are therefore removed by dialysis, the liquid treated with dilute acetic acid, and the precipitate removed by filtration; the filtrate of urine containing no albumin is now treated with a small quantity of blood serum (1.5 c.c. to a litre) and allowed to stand. The precipitate contains the nucleinic acid, together with chondroitin sulphuric and taurocholic acids (icterus). The presence of nucleinic acid is finally determined by determining the presence of phosphorus and of purin bases.

Allantoin.—This body is occasionally found in the urine of new-born children (during the first week of life), in the urine of pregnant women, and occasionally in the urine of men. It is a normal constituent of cat's, dog's, and rabbit's urine. It appears to be an intermediary product in the oxidation of uric acid; but it does not occur in the urine of man after excessive feeding with nuclein-containing food (Loewi). Its clinical significance is so small that methods for detecting and estimating allantoin will not be given.

Kreatin (*Kreatinin*).—Kreatin has occasionally been found in the urine of man. It is rapidly converted into kreatinin, however, and the latter substance is constantly found in the urine in quantities varying from 0.6 to 1.3 gm. in the twenty-four hours' quantity. It is derived from the disassimilation of muscle tissue either of the food or of the organism proper. In the muscles of the body kreatin is always formed first, and this is secondarily converted into kreatinin in its further passage through the blood and tissues. The excretion of kreatinin is chiefly dependent on the diet—much meat, much kreatinin. But even if all muscle meat is withheld, or if the meat is first leached out with water (Rubner) a certain amount of kreatinin continues to be excreted. Physical exercise seems to increase the kreatinin excretion.

Pathologically kreatinin has been found increased in febrile disorders of various kinds, and in diabetes. It has been found decreased in chronic nephritis, in diabetes insipidus, and in the period of convalescence from acute diseases, also in anæmia, chlorosis, tuberculosis. The clinical significance of a plus or minus in the kreatinin excretion is so far not understood. More casuistic data must be collected before this sign can be utilized in the interpretation of morbid states.

Tests.—Qualitative. Weyl's Test.—A small quantity of the filtered urine is treated with a few drops of a ten-per-cent. solution of sodium hydrate and one drop of a ten-per-cent. solution of sodium nitroprusside. If the urine contains kreatinin, it turns ruby red and then yellow. If the urine, after it has turned yellow, is now acidulated with acetic acid and heated, it turns green, then blue, and finally precipitates a blue sediment. This reaction does not occur in the cold. Instead of acetic acid certain other organic acids can be employed.

Kreatin does not give this test, neither do allantoin, xanthin, leucin, tyrosin, and other bodies that are genetically related to kreatinin. The only other urinary constitutent (with the exception of certain rare hydantoins) that gives a similar color test is *acetone;* on acidulation with acetic acid the liquid, however, turns red with acetone, whereas with kreatinin it turns blue. It is easy to drive off any acetone that may be present by first boiling the urine for a few minutes.

Test of Jaffé.—The urine is treated with a few drops of dilute sodium hydrate and a few drops of picric acid; the liquid at once turns red, even in the cold. This reaction can still be obtained in the presence of 1 part of kreatinin to 5,000 parts of water. No other known constituent of the urine gives this test.

Quantitative Determination.—Kreatinin forms a double compound with chloride of zinc—that is essentially insoluble in alcohol (1 to 9,217). This property is utilized for the quantitative determination.

Execution: Two hundred to 300 c.c. of urine are rendered alkaline with lime water and treated with a solution of calcium chloride so long as a precipitate continues to form. The mixture is allowed to stand for one or two hours and filtered. The filtrate is slightly acidulated with sulphuric acid and evaporated to a syrupy consistence in the water-bath. While still warm it is treated with 40 to 50 c.c. of alcohol of 95 per cent. The mass is thoroughly mixed washed into a beaker with a small quantity of 95-per-cent. alcohol and allowed to stand in a cool place for from six to eight hours. The precipitate is filtered off and washed and the filtrate and alcoholic washings evaporated back to about 50 c.c. This solution is now treated with 0.5 c.c. of an alcoholic chloride-of-zinc solution and allowed to stand for two or three days. The crystals of kreatinin-zinc chloride are then gathered on a weighed filter, repeatedly washed with alcohol until the filtrate shows no chlorine reaction, dried and weighed. One gram of kreatinin-zinc chloride represents 0.6242 gm. of kreatinin. In order, therefore, to determine the amount of kreatinin present in the quantity of urine employed for the determination, the figure obtained from weighing the zinc compound must be multiplied by 0.6242.

The reagent employed for precipitating the kreatinin-zinc compound (*i.e.*, the alcoholic solution of zinc chloride) is made by treating a saturated watery solution of zinc

chloride with alcohol until the mixture has a specific gravity of 1.200.

Oxaluric and Oxalic Acids.—Oxaluric acid occurs only in insignificant traces in normal urine, usually in the form of the ammonium salt. Oxalic acid is always present in normal urine. It usually occurs as the calcium salt, which is held in solution by diacid sodium phosphate. It precipitates with facility on standing and then forms characteristic crystals (see urinary sediments). Whereas oxalic acid $\begin{vmatrix} COOH \\ COOH \end{vmatrix}$ contains no nitrogen, it may nevertheless be discussed in this place in connection with oxaluric acid, as both these substances are chemically and, probably, genetically closely related. Oxaluric acid readily splits up into oxalic acid and urea according to the formula:

$$\begin{vmatrix} CO.NH \\ COOH.NH_2 \end{vmatrix} > CO + H_2O = \begin{vmatrix} COOH \\ COOH \end{vmatrix} + CO \begin{matrix} NH_2 \\ NH_2 \end{matrix}$$

Oxaluric acid. Water. Oxalic acid. Urea.

Both may be derived from uric acid, although oxalic acid may also be derived from other sources. It has recently been shown to be an intermediary produced in the degradation of dextrose. It may further be derived from certain articles of food, as asparagus, apples, grapes, and spinach. It is possible that a certain amount of the urinary oxalic acid is derived from this source.

The normal oxalic-acid excretion is about 0.02 gm. in twenty-four hours. Oxalic acid is occasionally found increased in diabetes. Some clinicians speak of vicarious oxaluria in this disease, for it seems that the sugar excretion decreases occasionally as the oxalic-acid excretion increases. If oxalic acid could ultimately be shown to be an oxidation or a splitting product of blood-sugar (see above), this peculiar relation would be easily explained. Oxaluria has finally been vested with the dignity of an independent clinical entity (oxalic-acid diathesis, idiopathic oxaluria). The syndrome of this condition is rather vague: the chief manifestations being a variety of subjective symptoms, emaciation, and a great increase in the excretion of oxalic acid (as much as 0.5 gm. in 1,000 c.c. of urine). No pathologic organic lesions are discoverable.

Estimation of Oxalic Acid. Qualitatively crystals of oxalic acid can be recognized by their solubility in HCl and their insolubility in acetic acid (see also "urinary sediments"). The quantity of oxalic acid is determined as follows:

Method of Neubauer.—The total quantity of the urine excreted in twenty-four hours is treated with calcium chloride and ammonia, then slightly acidulated with acetic acid and allowed to stand until the sediment settles at the bottom of the vessel. It is advised to add a few drops of an alcoholic thymol solution in order to prevent the excessive development of micro-organisms, for the latter may render subsequent clearing of the urine by filtration difficult. The precipitate is filtered off and placed into dilute hydrochloric acid together with the filter, the liquid heated a little, filtered, and the residue washed with water until the filtrate is no longer acid. The filtrate and washings are then evaporated to a small volume; while still hot this liquid is oversaturated with ammonia and colored with a few drops of litmus tincture as an indicator of the reaction. The solution is allowed to stand for twenty-four hours and the crystals of calcium oxalate gathered on a weighed filter; the weight of the filter ash must be known. The precipitate is washed free from chlorides, dried, incinerated in a platinum crucible and glowed to constant weight. This converts the oxalate of calcium into the oxide of calcium. Fifty-six parts of calcium oxide correspond to ninety parts of oxalic acid. The weight of the calcium oxide must, therefore, be multiplied by $\frac{90}{56} = 1.6071$, in order to give the amount of oxalic acid present in the total quantity of urine used for the estimation.

There are several sources of error in this method that render the results not quite accurate in the sense that too little oxalic acid is indicated. In view of the small quantities of oxalic acid excreted in the urine these small errors become relatively large. Other methods (Baldwin [Dunlop], Salkowski) in the writer's experience are fully as complicated as the old method of Neubauer, and no more accurate. In view of the slight clinical significance of small fluctuations in the oxalic-acid excretion and the small need of performing quantitative estimations these other methods will not be described in this article.

Carbohydrates.—Normal urine always contains small quantities of carbohydrates, notably the following three: animal gum, dextrose, and isomaltose. Chemically related to these are the conjugate glycuronates, and certain glucosides (chondroitin-sulphuric acid, nucleinic acid, and "mucin"). Occasionally pentose is also found in normal urine. Under pathological conditions the urine may contain levuloses (laiose) and certain polysaccharides, viz., erythrodextrin and glycogen.

Carbohydrates in General.—Certain reactions are common to all carbohydrates occurring in normal urine. They may consequently be utilized for the detection of these bodies.

(1) *The Benzol-ester Reaction* (*Baumann*). If the urine is shaken with benzoyl chloride and a quantity of sodium hydrate added sufficient to decompose the latter, a precipitate of benzoyl compounds is formed that incorporates dextrose, isomaltose, and animal gum.

(2) *The Furfurol Reaction.* Carbohydrates are decomposed by sulphuric acid, and one of the products of this decomposition is furfurol. The latter, even in very minute quantities, gives definite color reactions with certain reagents, viz., *a*-naphthol, thymol, xylidin, and resorcin. In addition to glucose, isomaltose, animal gum, and pentoses, albumen also gives this reaction with *a*-naphthol. In performing the test albumen should therefore be removed first.

(3) *The Reduction of Metal Oxides.* Normal urine reduces cupric and mercuric oxide in alkaline solution, and can also convert orthonitrophenyl propionic acid in alkaline solution into indigo blue. This method can hardly be utilized, however, to determine the presence of carbohydrates in normal urine. It is important merely to remember that normal urine, owing to the presence of certain reducing carbohydrate bodies possesses slight reducing powers, and that this factor must be included in determining the cupric-reducing powers of pathological urines.

Carbohydrates are commonly divided into monosaccharides, disaccharides, and polysaccharides. The di- and polysaccharides may be considered condensation products of monosaccharides with loss of water. Inversely di- and polysaccharides can be split by hydrolytic decomposition (addition of water) into the original component monosaccharide molecules.

Monosaccharides.—We distinguish among the monosaccharides trioses, tetroses, pentoses, hexoses, heptoses, etc., according to the number of carbon atoms the molecules contain. Of these different sugars the pentoses and the hexoses (*i.e.*, the sugars containing five and six combinations) are alone of physiological and pathological interest.

Pentoses. See article on *Pentosuria.*

Hexoses. Glucose (grape sugar, glycose, dextrose) $C_6H_{12}O_6$. As already stated, normal urine always contains traces of glucose. After the abundant ingestion of glucose, of disaccharides and polysaccharides, the excretion of monosaccharides (dextrose or levulose) in the urine may increase. This condition is called *alimentary glycosuria* (*e saccharo*).

Glycosuria (synonyms glycuria, melituria), *i.e.*, the excretion of dextrose in the urine, may occur in a great variety of conditions.

Certain drugs, as *uranium salts, corrosive sublimate, phosphoric acid* (intravenously), lead to the excretion of dextrose; certain other drugs, as *chloralamide, chloral, nitrobenzol,* and *nitrotoluol, orthonitro propionic acid,* lead to the excretion of reducing substances that are frequently taken for sugar. On careful examination it will be found, how-

ever, that these reducing substances rotate the plane of polarized light to the left, and are therefore not dextrose, and that they do not ferment with yeast, and are therefore not levulose. As a matter of fact, the bulk of these reducing substances consists of glycuronic acid compounds that these drugs form in their passage through the body. It is interesting to note, however, that in addition to these conjugate glycuronates, dextrose may appear in the urine at the same time.

Certain drugs that lead to cellular *asphyxia*, as *carbon monoxide, amyl nitrite, curare, methylsulphonal, strychnine, morphine, chloroform, ether*, and other drugs that produce asphyxia by narcosis, may all produce glycosuria.

Phloridzin produces sugar excretion in a different way than any of the other poisons enumerated. Whereas in all the glycosurias mentioned the excretion of sugar is preceded by the accumulation of abnormally large quantities of sugar in the blood, *scil.* hyperglycæmia, in phloridzin glycosuria the blood-sugar is not increased above normal. The exact pathogenesis of phloridzin glycosuria is still a subject of controversy. Phloridzin is a glucoside made from the bark of the roots of apple and cherry trees. On boiling with acids it decomposes into phloretin and phlorose, the latter being a monosaccharide that is closely related to glycose. One gram of phloridzin per kilogram of body weight administered to dogs by the mouth leads to the excretion of as much as eighteen per cent. of dextrose in the urine; the excretion of sugar may continue for two or three days after the administration of a single dose. In man von Mering caused the daily excretion of about 100 gm. of dextrose for thirty consecutive days by injecting 2 gm. of phloridzin every day. As soon as the exhibition of phloridzin was stopped, the excretion of dextrose also ceased.

Phloridzin glycosuria is without doubt due to some *renal* process. This is clearly shown by the absence of hyperglycæmia, even though the ureters are ligated or the kidneys extirpated. In fact, phloridzin injected into one of the renal arteries at first leads to the excretion of dextrose only from this one kidney; later the other kidney also begins to excrete sugar.

Two possible explanations can be proffered in the light of our present knowledge, viz.: either phloretin damages the renal epithelium in the sense that the latter becomes abnormally permeable for dextrose, or phloridzin is disintegrated into its two components in the kidney—the sugar component being excreted, the phloretin returning into the circulation, recombining with sugar to form phloridzin, and finally again undergoing decomposition in the kidneys. If the latter assumption is correct, the process of sugar excretion would be continued until finally the phloretin itself would be completely eliminated. A strong argument in favor of this theory is the observation that phloretin itself can produce glycosuria. In view of the fact finally that changes in the renal epithelia have never been observed after the administration of phloridzin, the latter pathogenesis is the one now almost universally accepted.

Glycosuria also appears after injuries to the *liver*, and in many chronic diseases of this organ. It may appear in the course of a great variety of *nervous disorders* (viz., apoplexy, brain tumor, encephalomalacia, cerebrospinal meningitis, dementia paralytica, multiple sclerosis, tabes dorsalis, traumatic neurosis, various functional neuroses, and in certain psychoses). In many of these disorders the sugar does not spontaneously appear in the urine, but only after the administration of carbohydrate pabulum in quantities so small that it would not lead to sugar-excretion in a normal subject. Here, then, the power of *assimilating* carbohydrate is merely reduced, hence the glycosuria.

Glycosuria may accompany *Basedow's disease, myxœdema, acromegaly*, and *Addison's disease;* sugar appears in the urine after the *injection of thyroid and suprarenal extracts.*

In *gout, obesity*, and *arteriosclerosis*, in certain *diseases of the pancreas*, in *syphilis*, in *cholera, malaria, carbuncle*, and other infections, sugar may appear in the urine.

Finally, glycosuria is the most typical symptom of *diabetes mellitus* and of *experimental diabetes* occurring in depancreatized animals.

Tests for Glucose. No simple test exists for the quantitative detection of glucose to the exclusion of all other sugars that may appear in the urine. From a clinical standpoint this differentiation is fortunately not very important; hence I will not describe the complicated methods we possess for isolating and identifying dextrose in a mixture of sugars and other carbohydrates and carbohydrate derivatives. Of the many urinary sugar tests we possess the following are the most practical and the most simple:

Fehling's Test (modification of Trommer's test).—Trommer's test was carried out as follows: The urine was rendered alkaline with potassium hydrate solution; a strong solution of copper sulphate was then added drop by drop until a portion of the cupric hydrate remained undissolved; the mixture was then heated. If appreciable quantities of sugar were present, yellow or red cupric oxide was precipitated even before the boiling point was reached, while at the same time the liquid became somewhat decolorized. This test is quite sensitive. Trommer was able to detect the presence of 0.001 per cent. of sugar. Unfortunately a large number of substances other than sugar can produce the same reaction—for instance, uric acid, kreatinin, allantoin, nucleoalbumin, bile pigments, conjugate glycuronates, etc. If the reduction occurs before the mixture is boiled, this reaction is always due to sugar. It only occurs, however, if the percentage of sugar is large.

Fehling modified this test by substituting a mixture of potassium-sodium tartrate (Rochelle or Seignette salts) and caustic alkali for the simple caustic alkali solution. Fehling's alkaline solution is made up as follows: 173 gm. of Rochelle salt and 120 gm. of sodium hydrate are dissolved in 500 c.c. of water. For quantitative work (see below) it is best to first prepare a sodium hydrate solution of 1.34 specific gravity and to dissolve 100 c.c. of this lye with 173 gm. of Rochelle salt in the necessary amount of water. The copper-sulphate solution should contain 34.63 gm. of copper sulphate to 500 c.c. of water. The two solutions should be kept separately. Before performing the test equal parts of the solutions are mixed and diluted with five volumes of water. As sugar is the only important urinary ingredient that reduces an alkaline copper solution at a temperature below the boiling point (*i.e.*, at about 80°), the author prefers to perform the Fehling test as follows: Equal portions of the urine and of the reagent are poured into two test tubes and each tube heated to boiling; both tubes are then allowed to cool off a little and the reagent then poured into the urine. If sugar is present, the yellow or red oxide of copper will appear almost at once and all through the liquid. This method of performing the test, aside from being more positive for sugar, is much more delicate for small quantities of dextrose.

Nylander's Bismuth Test.—This test is based on the same principle as the Trommer-Fehling test—*i.e.*, the power of dextrose to reduce metallic salts. Here the reduction of subnitrate of bismuth is utilized instead of the reduction of sulphate of copper. The test has this advantage over the Fehling test—that uric acid, kreatinin, and homogentisinic acid do not reduce bismuth subnitrate. After rheum, senna, salol, antipyrine, quinine, the urine, however, always gives this test. The presence of uroerythrin or of hæmatoporphyrin may simulate a reduction. If the urine contains much ammonia salt, the test may fail even in the presence of dextrose.

Nylander's reagent consists of 4 gm. of sodium and potassium tartrate, 2 gm. of bismuth subnitrate, and 10 gm. of sodium hydrate dissolved in 90 c.c. of boiling water. The solution, after cooling, must be filtered and preserved in a dark bottle.

Ten parts of the urine are treated with one part of the reagent and boiled for several minutes (at least two to three minutes!). It is imperative to *boil for some time.* If dextrose is present, a gray or dark-brown precipitate

of bismuthous oxide or a black precipitate of metallic bismuth will form.

Fermentation Test.—Glucose is split into alcohol, carbon dioxide, and certain other products (*i.e.*, succinic acid, glycerin, etc.) by the action of yeast.

$$\underset{\text{Glucose.}}{C_6H_{12}O_6} = \underset{\text{Alcohol.}}{2C_2H_6O} + \underset{\text{Carbon dioxide.}}{2CO_2}$$

According to this formula, which represents the chief reaction that occurs, a given quantity of sugar should yield 51.1 per cent. of alcohol and 48.9 per cent. of carbon dioxide. As a matter of fact, only 48.67 per cent. of alcohol and 46.54 per cent. of carbon dioxide are formed, the deficit being made up by 3.71 per cent. of glycerin and succinic acid and 0.94 per cent. of unknown substances. It will be seen, however, that the proportion between the two main products remains the same, viz., as 1.045:1 as called for by the equation. The temperature optimum for the alcoholic fermentation of sugar lies at 34° C. Below 15° C. the process is not completed, and above 45° C. it does not take place at all. Sugar solutions of from four to eight per cent. ferment more rapidly than more or less concentrated solutions. The proper proportion of CO_2 (46.54 per cent.) is only obtained if not more than one-half part of fresh doughy yeast is used for one part of sugar. More yeast leads to the development of more CO_2, owing to the auto-fermentation (development of buds) of the yeast that in itself leads to the generation of CO_2.

The test is performed as follows: A little compressed yeast is shaken with about 25 c.c. of urine and the mixture placed into a saccharometer (Einhorn's saccharometer). If glucose is present CO_2 will be developed at room temperature, or better at 34° C. The gas accumulates at the top of the tube. Before performing this test the yeast should be placed into a glucose solution in order to determine whether it is active. As normal urine frequently ferments a little, a control tube should be compared with the tube to be tested. If the percentage of sugar is very small, the CO_2 may be absorbed before it rises to the top of the tube. In case the urine gave a positive Fehling or Nylander test, but apparently does not ferment, it is well to repeat one of the reduction tests after the urine has been kept in the fermentation tube for twenty-four hours. If at the end of this time the urine no longer reduces copper or bismuth salts, then we may know that the original reduction was due to fermentable carbohydrate (glucose). If it still reduces Fehling's or Nylander's solution, then we may conclude that the original reduction was wholly or in part due to the presence in the urine of unfermentable carbohydrates.

The Phenylhydrazin Test.—This test was formerly considered quite pathognomonic for pathologic sugars in the urine. Since it has been shown, however, that normal urine, when treated with phenylhydrazin may occasionally precipitate crystals that resemble in appearance the typical glucosazon, the validity of this test seems impaired. The author, it is true, has never so far succeeded in obtaining such crystals from normal urine, but statements to this effect are made by competent authorities.

In addition to certain sugars (see below) the pentoses and glycuronic acids give osazons with phenylhydrazin. Acetone and diacetic acid give a hydrazin that is almost insoluble; oxalic acid gives a salt that is not very soluble; urea in concentrated urines gives a peculiar compound with phenylhydrazin. While acetone and oxalic acid will probably never be confounded with sugar, and while urea is probably never present in sufficient amounts in human urine to produce the formation of the phenylhydrazin compound, and while, finally, free glycuronic acid probably never occurs in the urine, nevertheless all these possible sources of error must be considered when interpreting the significance of a phenylhydrazin crystallization.

Our chief aid in differentiating the different osazons that are formed from various sugars is the melting point,* as this differs so considerably that the osazons can usually be distinguished by this means alone.

The test is performed as follows: 10 c.c. of urine are poured into a test tube and to it are added 0.5 to 0.75 gm. of phenylhydrazin, and not quite twice as much (1 to 1.5 gm.) of sodium acetate. With a little practice the amount of phenylhydrazin and the proportion of sodium acetate can be estimated with sufficient accuracy. The mixture is heated to boiling, and if all the salts do not dissolve readily, a little water is added. The tube is then placed into boiling water for from twenty to thirty minutes and then allowed to cool slowly. It is best to turn off the flame under the water-bath and to allow the tube to cool in the bath. At the expiration of half an hour the tube is placed into cold water. In this way better crystals are obtained. A number of rapid tests have been described; but I find the technique described above to be absolutely reliable, whereas I have on several occasions known the "five-minute tests" to fail; this applies particularly to urines containing only small amounts of sugar. As soon as the tube is placed into cold water, if not before, a yellow crystalline precipitate of phenyl-glucosazon appears. Sometimes this sediment appears amorphous on naked-eye inspection. On microscopic examination, however, it will be found to consist of fine needles that are arranged in bundles and sheaths. They are of a bright yellow color. The precipitate must present this microscopic appearance; flakes and plates of yellow material prove nothing in regard to the presence of sugar. In doubtful cases a melting-point determination of the crystals must be made. (For the technique see text-books on chemistry.)

This test can be performed even if the urine contains small quantities of albumin. Large quantities of albumin are preferably first removed by boiling and filtration. The test is very delicate and indicates the presence of 0.1 per cent. of sugar. The test requires a little practice, but after the technique is once mastered it constitutes one of the most satisfactory and reliable tests for sugar, particularly in combination with one of the reduction tests.

Polarimetric Examination.—For the qualitative recognition of glucose in the urine the polariscopic test is not very satisfactory because many other substances besides sugar can turn the plane of polarized light to the right or the left. The presence of glucose should, therefore, never be diagnosed from dextro-rotation alone. If a specimen of urine gives one of the above tests, and if in addition it shows marked dextro-rotation, this evidence may be considered highly corroborative of the presence of dextrose. Normal urine turns the plane of polarized light slightly to the left; albumen is also levorotary; biliary acids are dextrorotary. All these bodies can be precipitated from the urine by sugar of lead. This source of error can, therefore, be eliminated by treating the urine with sugar of lead and making a polarimetric examination of the filtrate; dextro-rotation may appear in the latter, whereas it was previously neutralized by the presence of levorotary substances in the urine. Other levorotary bodies that may mask the dextro-rotation produced by small quantities of glucose are levulose, conjugate glycuronates, and β-oxybutyric acid. If the urine is allowed to ferment and is examined with the polariscope before and after fermentation, the error introduced by the presence of these levorotary reducing substances may occasionally be detected and controlled (see Glycuronates below).

For a detailed description of the polarimeter and the technique of polarimetry I refer to special text-books on physics.

* *Melting Points of Various Osazons.*

Glucose	204-205° C.
Levulose	204-205° C.
Galactose	193° C.
Maltose	206° C.
Isomaltose	150-153° C.
Lactose	200° C.

There are many other qualitative tests for sugar, but their description lies beyond the scope of this article. The ones given are the best; they are sufficient for all clinical purposes.

Quantitative Estimation of Glucose.—By Titration. (*a*) According to Fehling.—In pure sugar solutions the sugar percentage can be determined by weighing the cuprous oxide precipitate. In the case of the urine this cannot be done because a portion of the oxide is held in solution by the ammonia that develops when urine is boiled with Fehling's alkaline solution. It is possible, however, to determine the volume of urine that is required to reduce the cuprous oxide salt in a definite volume of Fehling's solution. The correct volume of urine is determined by observing the exact point at which the blue Fehling's solution becomes discolored. In observing the color change one should not wait too long, but should examine as soon as the cuprous oxide begins to settle and leaves a narrow zone of clear fluid on top. If one waits too long, a bluish tinge may return owing to the oxidation of that moiety of the cuprous oxide that is held in solution by ammonia. In case the cuprous oxide does not settle rapidly the addition of some sodium hydrate hastens the precipitation.

The specific gravity of the urine having been determined in order approximately to estimate the amount of sugar it contains (see above), it should be diluted so far that it does not contain more than 0.5 per cent. It is good practice to always dilute diabetic urine five to ten times. The dilute urine is poured into a burette; 5 c.c. of the alkaline and 5 c.c. of the cupric solution (see above for Fehling's solution) are now mixed and diluted with 40 c.c. of water. The solution is heated to the boiling point and the urine allowed to flow into it slowly and carefully. A red or yellow precipitate of cupric or cuprous oxide forms and the blue color of the fluid disappears. The test should be repeated several times until the exact quantity of urine required to bring about the discoloration is determined to 0.1 c.c. A number of methods have been devised to determine the point of discoloration more accurately, but none of these methods have proven useful in the author's practice. For clinical purposes the above simple method is sufficiently accurate. In order to calculate the sugar percentage it must be remembered that each cubic centimetre of Fehling's solution corresponds to 5 mgm. of sugar; if 10 c.c. of Fehling's solution were reduced by a given quantity of urine, then this quantity of urine contained ten times 5 mgm., or 50 mgm., or 0.05 gm. of sugar. As the urine used for the test was diluted, the quantity of the original urine, that contains an equal amount of sugar, can be determined by dividing the cubic centimetres of diluted urine by the figure indicating how often the urine was diluted. For example, if 8.4 c.c. of diluted urine were required to reduce 10 c.c. of Fehling's solution, and if the urine was diluted six times, then the 0.05 gm. of sugar were contained in $\frac{8.4}{6}$ c.c. $= 1.4$ c.c. of the original urine; 100 c.c. of this urine, therefore, would contain 3.57 gm., or 3.57 per cent.

Method of Knapp.—This method does not require as much practice as Fehling's quantitative method. It is based on the fact that mercuric cyanide in alkaline solution is reduced by glucose to metallic mercury. In this test, too, however, there is an unavoidable source of error, for the urine always contains substances that can reduce the mercuric cyanide solution. For very accurate estimations the urine should, therefore, be fermented and its mercuric-reducing powers after fermentation determined. The figure obtained in this way should then be subtracted from the values for the total reducing powers; for ordinary clinical purposes this correction is superfluous.

For performing this test the urine should be freed from albumin by boiling with dilute acid and filtering. The urine should not contain more than one per cent. of sugar by a preliminary test or by estimation from the specific gravity; the sugar percentage should first be estimated, and, if the percentage is too high, the urine correspondingly diluted.

The reagent should contain 10 gm. of pure dry mercuric cyanide and 100 c.c. of sodium-hydrate solution of the specific gravity of 1.145 (or 13.3 gm. of sodium hydrate) to the litre. The reagent is conveniently made by dissolving 10.754 gm. of chemically pure mercuric chloride in a little water and adding so much cyanide of potassium that a drop of sodium-hydrate solution no longer produces a precipitate; to this mixture are added 100 c.c. of NaOH (specific gravity 1.145) as above. Then the whole is filled up to 1 litre.

Twenty cubic centimetres of this reagent are diluted with 75 to 85 c.c. of water. The dilution depends somewhat on the percentage of sugar in the diluted urine; the smaller the amount of sugar the less the dilution. The diluted reagent is heated to the boiling point and titrated with urine. From 1 to 3 c.c. of the urine should be allowed to flow in *at once* and the mixture boiled for half a minute after each addition of urine. As soon as approximately enough urine has been added to reduce all the mercuric cyanide, the mercury (and the phosphates) settle to the bottom and the liquid becomes clear. The reaction is complete when the supernatant fluid contains no more mercury salt. In order to determine the absence of the latter, a number of reagents have been recommended (viz., ammonium sulphide by Knapp, the originator of the method; sulphureted hydrogen by Leussen, and stannous oxide solution by Brumm). The writer has found the last-named indicator to be the best and uses it exclusively. The alkaline solution of stannous oxide is prepared by dissolving 50 gm. of stannous chloride in soda lye and diluting the solution to 1 litre. This reagent does not keep for a long time, as the stannous salt is soon oxidized. The addition, however, of a little metallic tin prevents this oxidation and preserves the reagent indefinitely. A drop of the clear supernatant fluid described above is placed on a porcelain dish and a drop of the stannous chloride solution added. If the fluid still contains mercury the drop turns gray; if it does not, it remains clear.

The calculation of the sugar percentage of the urine to be tested is based on the composition of Knapp's reagent; for the latter is compounded so that 20 c.c. correspond to 0.05 gm. of glucose. The calculation is similar to the one outlined above under "Fehling's test."

The Method of Pavy.—By the addition of ammonia to Fehling's solution the cuprous oxide formed in Fehling's test is held in solution, and the color change indicating the end-reaction is consequently not masked by the precipitate in suspension.

Pavy adds 300 c.c. of ammonia (specific gravity 0.880) to 120 c.c. of Fehling's solution, and fills the mixture up to 1 litre. Of this solution, from the Fehling's solution which it contains, 1 c.c. should indicate 0.6 mgm. of glucose. In reality, however, it only indicates 0.5 mgm. In other words, it is exactly 0.1 time as strong as Fehling's solution. The solution can be kept indefinitely. The above error, according to a later communication by Pavy, can be corrected by dissolving 20.4 gm. of potassium hydrate, 20.4 gm. of Rochelle salt, 300 c.c. of ammonia (specific gravity 0.880), and 4.158 gm. of copper sulphate in 1 litre of water; of this mixture 1 c.c. $= 0.5$ mgm. of sugar or 10 c.c. indicate 5 mgm. of sugar as the original Fehling's solution.

The titration should be performed with exclusion of the air. A small flask holding 80 c.c. is closed with a stopper with two perforations. Through the one hole passes the burette, through the other a U-tube filled with pumice stone that is saturated with dilute acid in order to bind the escaping fumes of ammonia. Ten cubic centimetres of the reagent are diluted with an equal volume of water and boiled for a few minutes until all the air is driven out of the flask. Then the diluted urine is allowed slowly to flow into the boiling reagent until discoloration is complete. This method is very convenient, very easy of execution, and sufficiently accurate to merit the universal popularity that it enjoys.

Other methods of quantitative sugar determination by titration have no advantages over the three described. They are, therefore, omitted.

By Fermentation. (*a*) Direct Determination.—With the aid of a saccharometer (see above), provided with a scale, the percentage of sugar may be read off directly, the amount of carbonic-acid gas developing during a stated time, at a certain temperature, and in urine diluted to a certain strength, indicating the amount of sugar disassociated by the yeast. The results of this test, even in complicated apparatus, are very inaccurate, for the sources of error are many. For clinical purposes of comparison, Einhorn's saccharimeter is nevertheless a useful instrument.

(*b*) Differential Density Determination before and after Fermentation.—The density of the urine before and after fermentation is determined and the difference in the densities multiplied by an empirical factor: the latter is obtained by dividing the figures for sugar (obtained by some other method) by the difference in the densities of such a stated sugar solution of known percentage before and after fermentation. It is known empirically that a diminution in the density of 0.001 corresponds to the loss of 0.234 per cent. of sugar by fermentation. In order to accelerate fermentation certain nutritive salts may be added to the urine. The best addition is a mixture of 2 gm. of Rochelle salts and 2 gm. of diacid potassium phosphate to each 100 c.c. of the urine; on addition of 10 gm. of compressed yeast to 100 c.c. of urine prepared in this way fermentation (at 30 to 34 c.c.) is usually complete within three hours. Before determining the specific gravity the suspended yeast cells should be precipitated by lead chromate; 100 c.c. of the urine are treated with 10 c.c. of a solution of neutral potassium chromate, saturated in the cold, and 10 c.c. of a solution of lead acetate. For purposes of comparison the original urine should be treated with the same precipitating mixture and the same nutritive salts, as the presence of these salts naturally changes the specific gravity. It has been found empirically, however, that the addition of 0.0178 to the specific gravity of the original urine corrects this error. The density determinations are best performed with the pyknometer, as aerometers do not, as a rule, give readings that are accurate for a sufficient number of decimal points. The difference in the specific gravities multiplied by 0.234 indicates the amount of sugar in per cent. If the urine contains more than 0.5 per cent. of sugar, this method yields excellent results. When less than 0.5 per cent. is present, the method is not so accurate.

Polarimetric Determination. See under qualitative tests; for the details I refer to text-books of chemistry and physics.

Levulose.—Two levuloses occur in human urine, *i.e.*, *fructose* and *laiose*. The former is the more important of the two.

Levulosuria (Fructosuria).—In the older literature a few isolated cases are on record of dextrosuria in which at the same time a small quantity of levulose was excreted. Quite recently Rosin and Labaud (*Zeitschr. f. klin. Med.*, 1902, vol. lxxiv, p. 182) have shown that considerable quantities of levulose are excreted in a large proportion of cases of diabetes, and that in addition there is a group of cases in which levulose alone is excreted, or in which only minimal quantities of dextrose are excreted together with large quantities of levulose. In the latter group of cases there is at the same time levulosuria.

The presence of levulose is not easy to detect if the urine at the same time contains much dextrose. The characteristic features of such urine are the following: The urine in the first place must give the so-called Seliwanoff reaction (see below). This indicates the presence of levulose (and of certain rare ketoses that need not be considered clinically). The reaction of the urine must be acid (diabetic urine that has not undergone decomposition usually *is* acid), for in alkaline urine dextrose seems spontaneously to undergo metamorphosis into levulose and mannose. In alkaline urine, therefore, the value of Seliwanoff's reaction as an indicator of levulose is impaired.

Seliwanoff's Reaction for Levulose.—Equal parts of urine, fuming hydrochloric acid, and a few grains of resorcin are rapidly heated; a deep red color appears and a dark precipitate forms that is soluble in alcohol with a bright red color.

In order to determine, in the second place, the proportion of levulose to dextrose the following plan may be pursued: The sugar of the urine is, first, determined by use of the reduction tests, and, second, by polarization. If there is a considerable difference in the amount of sugar indicated by these two tests, if, *e.g.*, more sugar is indicated by reduction than by polarization, then the urine is subjected to fermentation until no rotation can be obtained and until the reaction of Seliwanoff is negative. If the reducing power of the urine disappears at the same time, then the difference between the figures obtained from reduction and polarization of the original urine must be attributed to the presence of considerable quantities of levulose, for no other urinary substance excepting fructose (levulose) is fermentable and gives Seliwanoff's reaction at the same time.

The following example (quoted from Rosin and Labaud, *loc. cit.*) may illustrate the method:

Case IV.—Urine gives marked Seliwanoff reaction. Titration (Fehling) indicates 7.1 per cent., polarization 6.4 per cent. After fermentation: Seliwanoff reaction negative, polarization 0. Titration: The urine contains less reducing substance than would correspond to 0.1 per cent. dextrose. Difference between titration and polarization, 0.7 per cent.

The presence of levulose in many cases of diabetic urine may aid in explaining the well-known fact that titration of diabetic urine so frequently indicates higher values for sugar (dextrose) than polarization. We must imagine that the tendency of the dextrose to rotate the plane of polarized light to the right is in part neutralized by the opposite tendency of the levulose present in such urines to rotate it to the left.

Other reducing bodies like pentose and glycuronic acid occur in too small quantities to impair the validity of the viewpoint enunciated above. Urines, moreover, that do not give Seliwanoff's reaction do not reveal the differences described. Levulose, therefore, is in all probability the chief and only cause. Rosin and Lebaud succeeded in strengthening this view by manufacturing levulose as such from urine giving the above tests (they employed the method of C. Neuberg, *i.e.*, they precipitated the levulose with methyl-phenylhydrazin as a methyl-phenylosazon).

Other methods have been proposed to determine the presence of levulose in diabetic urines; but all of these are complicated, and, moreover, ambiguous; none of them gives results that are so conclusive as the above method, so that they will not be discussed in this article.

Laiose (Syn: Leo's Sugar). This sugar was found by Leo in three out of twenty-one diabetic urines. Here, too, titration revealed from 1.2 to 1.8 per cent. more sugar (calculated for dextrose) than polarization. In order to identify this interesting sugar it must be isolated from the urine as follows:

The urine is treated with lead acetate and the lead precipitate filtered off; the filtrate is treated with ammonia; the precipitate contains laiose and dextrose. It is washed out with water and decomposed with H_2S; the lead sulphide is filtered off and the filtrate evaporated to a syrupy consistence in the vacuum over concentrated H_2SO_4. The syrupy residue is dissolved in methyl alcohol and the dextrose precipitated by a solution of barium hydrate in methyl alcohol. So much of the reagent should be added that the liquid becomes alkaline. The mixture is filtered, the ammonia removed by placing the dish under a bell jar or over H_2SO_4. This leads to the precipitation of barium carbonate and some barium dextrose. The barium is removed from the filtrate by CO_2. The methyl alcohol is removed by distillation in vacuo; the residue

is dissolved in water. It contains any laiose that may be present.

Laiose is distinguished from other sugars by the following properties: It is not so sweet as dextrose; has smaller reducing powers, and does not ferment so actively. It has a specific rotatory power, and it forms a compound with phenylhydrazin. Although laiose possesses all these properties that seem to class it with the sugars, it is not identical with any known sugar. In fact, it appears doubtful whether it is a hexose or a pentose. (See also Leo: *Virchow's Archiv*, vol. cvii., p. 108, 1887).

Disaccharides.—Isomaltose has been isolated from the urine in small quantities. It is precipitated with other carbohydrates as a benzol ester when the urine is treated with benzoyl chloride (see above, page 38). It is possible that it is formed from dextrose in process of isolation. This sugar is clinically altogether unimportant.

Lactose (*Sugar of Milk*).—This sugar is found in small quantities in the urine of nursing women if there is stasis of milk ("lactosuria"). After the ingestion of 100 gm. of lactose this sugar may appear in the urine of men, or of women who are not nursing. On an abundant milk diet lactose may also appear in the urine. In diabetics the ingestion of lactose leads to the excretion of dextrose. Inversely in nursing women excessive quantities of dextrose (150 gm.) may lead to the excretion of lactose. In new-born children with gastric catarrh lactose has been found in the urine.

Tests. Rubner's Test.—The urine is boiled for two or three minutes with an excess of lead acetate. If lactose is present, the liquid turns yellowish-brown; the precipitate that forms is dissolved in a little ammonia. The liquid now turns brick-red. On standing, a cherry-red or copper-colored sediment settles at the bottom of the tube, while the supernatant fluid becomes clear and colorless. If dextrose is present, this test cannot be applied because a similar reaction is obtained with this sugar. Sometimes lactose and dextrose can be differentiated by heating the urine gently to about 80° (not to boiling). If lactose alone is present, the liquid will not turn red, but yellow or brown, whereas if dextrose alone is present it will turn red.

Fermentation Test.—Lactose does not ferment, but it reduces metal oxides. If, therefore, the urine after fermentation still possesses reducing powers, the presence of lactose may be suspected if the case is a woman in the puerperium, or if the subject is living on a milk diet. The test is by no means, however, conclusive, for lactose, as other non-fermentable sugars, notably pentoses, may be present. In order fully to identify lactose it must be isolated from the urine (see Hofmeister, *Zeitschr. f. phys. Chem.*, vol. i., p. 105).

Polysaccharides.—Animal Gum (Syn.: *Achroglycogen, Urinary Dextrin*). Animal gum is always present in the urine. It is precipitated as a benzol ester with benzoyl chloride (see page 38.) In certain chronic disorders animal gum is increased. Together with isomaltose (that is also precipitated by benzoyl chloride) urinary dextrin forms the group of *unfermentable urinary carbohydrates*, a class of bodies that are attracting much attention and that promise to attain considerable clinical importance.

Animal gum can be isolated from the benzoyl chloride precipitate that forms in a mixture of the urine and sodium hydrate by a complicated method that is described in detail in Huppert's "Harnanalyse," p. 144, 1898. The body is not of sufficient interest for the present to warrant a full description of this method in an article of this limited scope.

Glycogen (Erythrodextrin?). In the urine of diabetics a body is occasionally found (particularly after the dextrose has been caused to disappear) that gives a brown color with iodine. Such urine reduces Fehling's solution only after prolonged boiling. This body has so far never been found in the urine of healthy subjects. From the material published so far it is impossible to determine whether this body is glycogen or erythrodextrin. On physiologic grounds presumptive evidence is in favor of the former supposition.

To test the urine for glycogen (erythrodextrin) a first specimen should be treated with several volumes of alcohol. The alcoholic precipitate, if the urine is diabetic, should be freed from sugar by repeated washing with alcohol or by repeated solution in water and reprecipitation with alcohol. Certain portions of the precipitate, if glycogen is present, assume a brown tint if treated with iodine. By boiling the precipitate for half an hour with ten-per-cent. H_2SO_4 any glycogen or erythrodextrin that may be present is hydrolyzed and converted into dextrose, and the latter, after neutralization of the liquid with sodium hydrate solution, will reduce Fehling's solution, give a phenyl glucosazon, and (after removal of salts by dialysis) ferment (method of Leube).

Aromatic Constituents.—The aromatic constituents of the urine are derived from the degradation of albumins. These degradation products may either enter the body preformed in the food, or they may be formed in the gastro-intestinal tract by bacterial putrefaction, or they may be formed in the tissues proper with or without the intervention of bacteria. Occasionally these aromatic bodies appear in the urine as such. As a rule, however, they appear in combination with sulphuric acid, glycuronic acid, or glycocoll, so that we can conveniently subdivide the combined aromatic constituents of the urine into three groups, viz.: (1) *the conjugate sulphates*, (2) *the compound glycuronates*, (3) *the compound glycocolls*. A fourth group of aromatic bodies, *i.e.*, the aromatic oxyacids, more frequently occurs as such and not combined, so that these substances will be discussed separately under the heading of (4) aromatic oxyacids.

(1) *Conjugate Sulphates.*—The conjugate sulphates include the following bodies: Phenols (kresol, pyrocatechin, hydroquinon), indol (indican), and skatol. Of these bodies the majority are eliminated as the sodium or potassium salt of the ethereal sulphates (*e.g.*,) ($HO.C_6H_4.SO_2OK$). Indol and skatol, however, are not eliminated as indol or skatol sulphuric acid salt, but undergo preliminary oxidation to indoxyl and skatoxyl, and consequently appear in the urine as indoxyl sulphuric acid (indican) or as skatoxyl sulphuric acid. The most important member of this group is *indican*. The amount of ethereal sulphates excreted in man varies according to the character of the food, the ingestion of certain drugs that are excreted as ethereal sulphates (carbolic acid, *scil.* phenol, etc.), the degree of putrefaction going on in the intestine, the character of the putrefactive bacteria, and the existence of certain morbid conditions of the system that lead to perverted tissue metabolism. The total average quantity of conjugate sulphates approximately equals 0.1 of the mineral sulphates, *i.e.*, on an ordinary mixed diet from 0.15 to 0.3 gm. of SO_3. We do not know where in the body the synthesis of the aromatic conjugate sulphates occurs.

The presence of aromatic ethereal sulphates can be detected as follows: Not less than 25 c.c. of urine are acidulated with acetic acid and the mineral sulphates precipitated with barium chloride. The precipitate of barium sulphate is filtered off and the filtrate heated with hydrochloric acid. As the ethereal sulphates are not precipitable by barium chloride and as they can be decomposed by heating with hydrochloric acid, the mixture now contains ordinary sulphuric acid and alcohols derived from the splitting of the ethereal sulphates. In this liquid the liberated sulphuric acid can be precipitated by barium chloride, so that the appearance of a barium sulphate precipitate speaks for the presence of conjugate sulphates in the original urine. This method can also be employed for the quantitative determination of the conjugate sulphates (see paragraph on "Sulphates" under Inorganic Constituents).

Phenols.—The most important of the phenols is parakresol. Phenol itself is less abundant, and pyrocatechin and hydroquinon are excreted only in very small quantities.

Phenol.—Phenol given by mouth appears as conjugate sulphate. If more is given than can be combined with

available sulphuric acid, the excess appears as compound glycuronate (see below). Phenol is not found in the urine of the new-born, because their intestine is sterile, nor is it found in the urine of animals whose intestine is maintained sterile from birth. All local putrefactive and gangrenous processes lead to the elimination of urinary phenol.

Phenol appears in quantities that vary from 0.017 to 0.5 gm. (Munk) in the urine. The average excretion is 0.03 gm. It is more abundant on a vegetable than on an animal diet. Phenol is increased in all conditions of coprostasis, particularly in the lower portions of the small intestine and in the colon; in peritonitis, in pyæmia, in suppurative processes, in phosphorous poisoning, and in diabetes mellitus. Tyrosin and benzol given by mouth also lead to increased phenoluria. When the urine contains much indican, it also always contains much phenol; but the reverse is not the case. As the methods employed for determining phenol also include kresol, the figures given really indicate the combined excretion of the two aromatic alcohols.

Detection: Phenol itself gives a large number of very sensitive tests. Unfortunately, however, more of these reactions give satisfactory results with phenol as conjugate sulphate, *i.e.*, with urinary phenol. In order to detect its presence the phenol must first be liberated as follows: One litre of urine is treated with so much H_2SO_4 that the strength of the mixture is five per cent. The solution is then distilled until the distillate gives no clouding with bromine water. This distillate contains phenol. The following tests can be performed: (*a*) Bromine water is added until the solution is yellow; on standing a crystalline, yellow precipitate of tribromphenol is deposited. (*b*) Millon's reaction is positive (Millon's reagent: Mercury is dissolved in an equal portion by weight of sixty-three per cent. $HNO_3(4HNO_3 + 3H_2O)$ first in the cold, then by warming. One volume of this solution is diluted with two volumes of water and the precipitate that forms filtered off. The clear filtrate is the reagent). With phenol this reagent gives a rose-red color. (*c*) Phenol treated with sodium hypochlorite gives a blue color; care must be taken not to add too much hypochlorite. (*d*) Heating phenol with iodine and sodium-hydrate solution to 50 to 60° C. gives a dark-red amorphous precipitate of triiodine phenol. The latter reaction has been employed in a quantitative method for determining phenols, the amount of mono-oxybenzols being calculated from the amount of iodine that is employed. The method is complicated and does not indicate individual phenols, but merely the phenols as a group. The reaction that occurs may be schematized by the equation:

$$\underset{\text{Phenol.}}{C_6H_5OH} + \underset{\text{Iodine.}}{6I} = \underset{\text{Triiodine phenol.}}{C_6H_2I_3OH} + \underset{\text{Hydriodic acid.}}{3HI}$$

Kresol.—Kresol, as has already been stated, is the most abundant of the phenols. Much that has been said of phenol, particularly in regard to occurrence and detection and estimation, applies with equal force to kresol. Kresol is a methylated phenol. The relation between the two may be illustrated by the formulas: $H.C_6H_5.OH$, phenol, $CH_3.C_6H_5.OH$, kresol.

There are three kresols that are isomeric, viz., parakresol, orthokresol, and metakresol, as the substituting methyl group may occupy any one of three different positions in the phenol ring. Of the three isomers parakresol is the most abundant in man; some orthokresol is usually also present. Metakresol has so far not been found in human urine, but it occurs in horses. The differentiation of kresols from phenol is possible, but the process is complicated. Clinically this differentiation is unimportant; hence it will not be described.

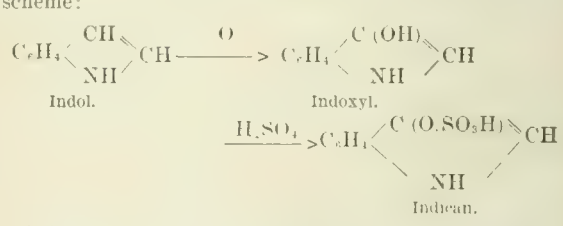
Pyrocatechin, $C_6H_4(OH)_2$.—This is a constant constituent of human urine. It is derived from pyrocatechu acid, that is of common occurrence in many plants. It is excreted after the administration of carbolic acid or of benzole.

Urine containing pyrocatechin soon turns dark on standing, provided the reaction is alkaline. The presence of pyrocatechin may be suspected if this change in the urine occurs, but hydroquinone and alkaptonic acid (see below) produce a similar change. A few drops of chloride of iron added to the urine give a dark green color if pyrocatechin is present. If a little tartaric acid is added and the mixture is treated with ammonia, the urine first turns violet and on addition of more ammonia cherry-red.

Hydroquinone, $C_6H_4(OH)_2$.—This body only occurs in the urine after the administration of carbolic acid (phenol), benzol and hydroquinone itself. It always appears as conjugate sulphate. Urine containing hydroquinone turns dark on standing. If urine containing hydroquinone is boiled with a dilute solution of iron chloride, quinon is formed, and this body can readily be recognized by its penetrating odor.

As pyrocatechin and hydroquinone frequently appear in the urine after carbolic-acid poisoning, it is important occasionally to isolate them from the urine in order positively to demonstrate their presence. For this purpose the urine is acidulated with hydrochloric acid, heated for half an hour on the water-bath, and after cooling extracted with ether. The ethereal extract is repeatedly shaken with sodium-carbonate solution, the ether evaporated and the residue treated with small quantities of a saturated sodium chloride solution. This salt solution takes up the pyrocatechin or hydroquinone that may be present. The solution is diluted with water and distilled to remove volatile phenols. The residue is again extracted with ether and the ether evaporated; the residue is dissolved in water and precipitated with lead acetate; the precipitate contains the pyrocatechin, while the hydroquinone remains in solution. The precipitate is decomposed with H_2SO_4 and extracted with ether. From this ethereal solution pyrocatechin crystallizes in prisms. The solution containing hydroquinone is treated with H_2SO_4, heated with barium carbonate, and the filtrate extracted with ether. From the ethereal extract hydroquinone crystallizes in the form of rhomboid crystals that can be recrystallized from benzol and melt at 160°.

Indoxyl (*Indican*), C_8H_7NO. Indican, the sulphate of indoxyl in combination with sodium or potassium, was originally believed to be identical with vegetable indican, the chromogen of the indigo plant. It has been shown, however, that animal indican is derived from indol and is the ethereal sulphate of indoxyl, an oxidation product of indol, while vegetable indican is a glucoside of the formula $C_{26}H_{31}NO_{17}$. The relation of indol, indoxyl, and indican may be illustrated by the following scheme:



Indol, like the phenols, is a product of the putrefaction of albumin somewhere within the organism. Consequently, we always find phenol in abundant quantities whenever indican is excreted in the urine. Inversely, however, the presence of phenol does not necessarily indicate the presence of indican. In the new-born indican is never found in the urine. In adults it is always present in small quantities. From 2 to 50 mgm. of indigo-blue can be isolated from the twenty-four hours' urine on a mixed diet. A meat diet leads to an increase of the urinary indican, and a vegetable diet to a decrease. Pathologically indicanuria is increased in all conditions that favor abnormal intestinal putrefaction, particularly if there is at the same time some stasis of the intestinal contents. Thus marked indicanuria is common in ileus, typhoid, acute and chronic peritonitis, intestinal tuberculosis. In cholera, gastric ulcer, gastrectasis, gastro-

intestinal catarrh, lead colic, perityphlitis and appendicitis indican has also been found increased in the urine. Occlusion of the colon does not lead to increased indicanuria. Large quantities of indican have finally been reported in cases of carcinoma of the liver, the stomach, the uterus, in empyema and putrid bronchitis, and in melanosis. Fever *per se* exercises no effect on the excretion of indican. Opium does not increase indicanuria. Laxatives, however, reduce it.

It will be seen, therefore, that indicanuria is a normal phenomenon, and that the excretion of large quantities of indican is a very common sign. Diagnostically, therefore, the appearance of abnormally large quantities of indican in the urine indicates merely that there is abnormal putrefaction of albumin somewhere in the body. Further than this we can rarely go, and it is a precarious matter to make a special diagnosis on the basis of increased indicanuria, for we must never forget that simple coprostasis may lead to a great increase of the urinary indican.

Other products of indoxyl that may appear in the urine are indigo red (indoxyl *plus* isatin), indoxyl glycuronic acid (see above), and a variety of more or less defined pigments that are variously known by the names urohæmatin, urrhodin, urorubin, indirubin, indigo-purpurin, etc.

Tests for Indican. 1. Jaffé's Test.—Hypochlorite of sodium oxidizes indican in acid solution to indigo blue. This pigment is soluble in chloroform. Equal parts of the urine and of concentrated hydrochloric acid are mixed in a test tube, and to the mixture are added a few cubic centimetres of chloroform and, drop by drop, a dilute solution of sodium hypochlorite. On the addition of each drop of the latter reagent the mixture should be thoroughly shaken. The layer of chloroform will gradually turn blue. Care must be taken not to add too much of the hypochlorite, as otherwise the indigo blue is oxidized further, and is converted into a colorless compound. Instead of using hypochlorite, the oxidation may also be performed with dilute chlorine or bromine water. If the urine contains albumin, the latter must first be precipitated by lead acetate and the test performed in the filtrate. If the urine is very dark, it may also be decolorized by precipitation with lead acetate.

2. Obermayer's Test.—As chloroform forms an emulsion with the urine that frequently renders it difficult to recognize the blue color of the indigo in chloroform solution, Obermayer first precipitates the urine with lead acetate, filters, oxidizes the indican in the filtrate with ferric chloride in concentrated hydrochloric acid, and then shakes out the indigo with chloroform. The blue solution then settles at the bottom of the tube. An excess of lead acetate must be avoided, otherwise lead chloride will precipitate when the hydrochloric acid is added, and this would render the chloroform cloudy. The addition of lead acetate has the additional advantage of removing bile pigment that may be present in the urine.

The filtrate from the lead-acetate precipitate is shaken with an equal volume of fuming hydrochloric acid containing 3 gm. of ferric chloride to the litre. The mixture should be agitated for about two minutes.

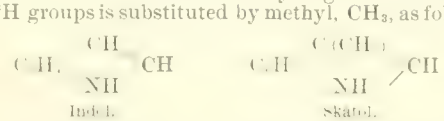
Quantitative Estimation of Indican.—Obermayer's test can be utilized for the quantitative determination. The urine, after treatment with Obermayer's reagent (3 gm. iron chloride to 1 litre of fuming hydrochloric acid) is repeatedly extracted with chloroform. In the chloroform solution the amount of indigo-blue can be determined: (*a*) by weighing, (*b*) colorimetrically, (*c*) spectrophotometrically.

(*a*) By Weighing.—The chloroform is driven off in a weighed dish and the residue dried at 110° C. and weighed.

(*b*) Colorimetrically.—The chloroform solution is compared with solutions of pure indigo-blue in chloroform of known percentage. By diluting the urinary chloroform extraction with measured quantities of chloroform until its color corresponds exactly to that of one of the standard tubes, the amount of indigo-blue in the urine can be estimated by a simple calculation.

(*c*) Spectrophotometrically (F. Müller).—This method requires much practice and a complicated apparatus, a spectrophotometer. I refer for a description of the method to Huppert, "Harnanalyse," p. 692 *ff.*). This method is not any more accurate than those given under (*a*) and (*b*).

Skatoxyl. This body is an oxidation product of skatol, and skatol is indol in which one hydrogen atom of one of the CH groups is substituted by methyl, CH_3, as follows:

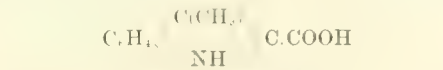


Indol. Skatol.

Skatoxyl combines with sulphuric acid, and appears in the urine as the sodium or potassium salt of skatoxyl-sulphuric acid. If more skatol is formed than can be combined with available sulphuric acid, the excess appears in the urine as skatoxyl glycuronic acid (see below). Skatol is a normal constituent of human fæces; whether it occurs normally in the urine remains doubtful for the present. This is due to the fact that the only qualitative index of the presence of skatol (skatoxyl) in the urine is the appearance of a red pigment when the indican tests are performed, and this red pigment may be indigo-red and due to the presence of indican. Skatoxyl sulphuric acid has been found in large quantities in cases of diabetes suffering from digestive disorders. It is possible that some of the many red pigments that have been found in the urine by many different observers are skatol derivatives.

The presence of skatol can be suspected if the urine turns dark on standing: the color usually becoming dark reddish or violet, or even black. If Jaffé's indican test is made the addition of hydrochloric acid alone will color the urine dark red or violet; nitric acid alone or with the addition of a little potassium nitrate produces a cherry-red color; ferric chloride with or without hydrochloric acid also a cherry-red color. The pigment separates out on boiling, and can be extracted with ether. These color tests unfortunately are not typical for skatol, for similar reactions are given by indol red. For order to differentiate the two the pigment must be precipitated from the urine, according to the method adopted in Jaffé's indican test; the pigment is then treated with zinc powder and indol or skatol liberated in this way. Numerous tests are given that are more or less typical for either body. If enough indol or skatol is present to yield a few crystals, the difference in the melting points may decide (indol 52° C., and skatol 95° C.). For other tests I refer to Huppert, "Harnanalyse," pp. 169 and 170).

Skatol can appear in the urine as skatoxyl sulphuric, skatoxyl glucuronic, and skatoxyl carbonic acid. The chemistry and formation of the former is analogous to that of indoxyl sulphuric acid, and much that has been said in regard to indol and its urinary congeners applies with equal force to skatol. Skatoxyl glycuronic acid forms if more skatoxyl is thrown into the circulation than can be combined with available sulphuric acid. This compound glycuronate will be presently discussed. Skatoxyl carbonic acid is never present in large quanti-



Skatoxyl Carbonic Acid.

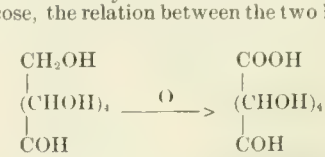
ties. It gives the ferric chloride reaction with hydrochloric acid or hypochlorite in the urine direct. In order to demonstrate its presence it must be isolated from the urine. As the clinical significance of this substance is not very great, the method of Salkowski (*Zeitschr. f. phys. Chem.*, vol. ix., 32) will not be described in this place.

Conjugate Glycuronates.—Glycuronic acid does not occur free in the urine, but only in combination with certain aromatic bodies, as phenol, paracresol, indoxyl, and

skatoxyl (see above), certain drugs, as naphthol, camphor, toluol, menthol, oil of turpentine, morphine, chloral, and many others. Some of these bodies appear only in combination with glycuronic acid, others, as the phenols, combined first with all the available sulphuric acid to conjugate sulphates, and with glycuronic acid, only after all the supply of sulphuric acid is exhausted. The resulting compounds partake of the character of glucosides.

The conjugate glycuronates are monobasic acids; all rotate the plane of polarized light to the left. The different members of this group, however, show individual peculiarities in other respects. By hydrolysis the glycuronates can be split into free glycuronic acid and the component alcohol. In some cases this disassociation occurs on gentle heating or even at ordinary temperatures, whereas in others boiling with dilute acids or heating with superheated steam is necessary. Some of the conjugate glycuronates reduce cupric oxide in alkaline solution; others do not. Some are precipitable by lead acetate and others are not. These differences are determined by the character of the alcohol in combination with the glycuronic acid molecule.

Glycuronic acid may be considered an oxidation product of glucose, the relation between the two being the following:



Glucose. Glycuronic acid.

As the greater portion of the glucose circulating in the blood is derived from the stored glycogen, it may be said that glycuronic acid is derived from glycogen *viâ* glucose. The acid must be formed in the tissues of the body, for if camphor or chloral, *e.g.*, are administered to a starving animal these bodies will appear in the urine as glycuronates. It is very probable, therefore, that glycuronic acid in this case is derived from the stored glycogen in the liver and muscles. If glycuronic acid, moreover, is fed to animals, the glycogen content of the liver is apparently spared, for after such feeding the liver glycogen increases. Another possible source of glycuronic acid is chondroitin-sulphuric acid (see under "Mucin"), for the latter can be split into glycuronic acid and glycosamin *viâ* chondrosin by a process of hydrolytic disassociation.

Free glycuronic acid and its salts rotate the plane of polarized light to the right, whereas, as we have seen, the aromatic glycuronates are levorotatory. As the free acid, its salts and esters, can reduce metal oxides, glycuronates may readily be taken for glucose. This confusion may be still more enhanced if phenylhydrazin compounds are made, for the free acid forms a crystalline phenylhydrazin compound that melts between 114° and 115° C. Glycuronic acid is not, however, fermentable.

Glycuronates will only be looked for in urine that is levorotatory. In order to demonstrate the presence of glycuronic acid, the latter must be liberated from its compounds. This can be done as follows:

Fifty cubic centimetres of the urine are treated with so much dilute sulphuric acid that the strength of the resulting mixture equals one per cent. The solution is heated over the free flame in a porcelain dish in order to bring about the disassociation of the various glycuronic acid compounds. Boiling for two or three minutes is sufficient. Without filtering, the *orcin test* is performed as follows: A saturated solution of orcin in concentrated hydrochloric acid containing a slight excess of orcin is the reagent. A few drops of this reagent are added to the above mixture and the solution boiled for one or two minutes; a red color should appear. If it does not appear after two minutes' boiling, it is useless to boil longer, for by prolonged boiling any glycuronic acid that might have been present would be decomposed. The orcin test can only be considered positive if certain characteristic absorption bands are found in the spectrum (see Salkowski: *Zeitschr. f. phys. Chem.*, 1899, No. 27).

In diabetes the appearance of glycuronic acid has attracted much attention of late years. As glycuronic acid is an oxidation product of glucose that may be considered intermediary between glucose and the terminal products of its disassimilation, viz., CO_2 and H_2O, the appearance of glycuronic acid in the urine of diabetics has been interpreted to signify incomplete oxidation of sugar. Several writers go so far as to claim that a "delayed Fehling test" in urine that is free from glucose but that contains glycuronic acid is evidence of deficient sugar destruction, and should be considered a warning of impending glycosuria and diabetes. This field is promising and the above hypothesis very seductive. The subject is not sufficiently worked out, however, to merit elaborate discussion in this place. I content myself with referring to it thus briefly. In looking for glycuronic acid in diabetic urine the sugar should first be removed by fermentation. If the liquid is levorotatory after fermentation, the presence of glycuronic acid or its compounds may be suspected; if it still reduces Fehling's or Nylander's solution, and if it gives the orcin reaction after boiling with one-per-cent. sulphuric acid, the existence of glycuronic acid may be considered demonstrated.

Compound Glycocolls.—Glycocoll is amido-acetic acid. It combines with certain aromatic decomposition products of the albumins that are formed in the intestinal tract by putrefaction or in the proper tissues by perverted katabolism—the resulting compounds appear in the urine as compound glycocolls. The two most important members of this group are *hippuric acid* and *phenaceturic acid*, the former a compound of phenylpropionic acid (after its oxidation to benzoic acid) with glycocoll, the latter a compound of phenylacetic acid with glycocoll.

Hippuric Acid. The source of the glycocoll entering into the composition of hippuric acid is obscure. It may be formed from albuminous putrefaction, as all albumins contain a glycocoll radical. The phenylpropionic acid and its oxidation product, benzoic acid, are derived from the degradation of albumins by intestinal putrefaction. In addition certain articles of diet—in particular, certain vegetables—contain bodies like cinnamic and quinic acid, toluol, etc., which may lead to the formation of benzoic acid. We find, therefore, that the elimination of hippuric acid is greater on a vegetable diet than on a meat diet, greater in herbivora than in carnivora. The excretion of hippuric acid in carnivora is exclusively due to the intestinal putrefaction of albumins. In man the ingestion of cranberries, plums, prunes, leads to an increased excretion of hippuric acid. The total hippuric-acid excretion may fluctuate from 0.1 to 1 gm. a day. The normal average excretion on an ordinary mixed diet containing more of the above-named fruits may be placed at 0.6 gm.

Test.—In order to demonstrate the presence of hippuric acid in the urine it is necessary to isolate it. The best method for the isolation of hippuric acid on a small scale is that recommended by Bunge and Schmiedeberg. About 500 c.c. of the urine are rendered alkaline with sodium carbonate, evaporated almost to dryness, and the residue repeatedly extracted with alcohol. The alcohol is driven off, the watery residue acidified with HCl and repeatedly extracted with acetic ether. The acetic ether extract is decanted off and washed with water, then evaporated at a low temperature. The residue contains hippuric acid and any benzoic acid or fat that may be present in the urine. If the residue is treated with petroleum ether, these impurities can be removed and pure hippuric acid remains behind. The hippuric acid is then crystallized from warm water at 55° C.

The crystals of hippuric acid can be recognized from their form, for they constitute milk-white, semitransparent, quadrilateral prisms and columns that are frequently united to form rosettes. On dry distillation (*i.e.*, on heating in a dry test tube), hippuric acid first melts to an

oily fluid (that again becomes crystalline on cooling), that gradually turns red if the temperature is raised sufficiently, and finally gives off benzoic acid that sublimes on the walls of the test tube and emits an agreeable odor at first of hay, later of prussic acid. The crystals of hippuric acid are very soluble in alcohol and hot water, and this property, too, may aid in identifying them. Confusion with phenaceturic acid (see below) can be avoided by performing a melting-point determination (melting point of hippuric acid 187.5° C.; melting point of phenaceturic acid 143° C.).

Phenaceturic Acid. This body is only rarely found in the urine of human subjects, but is common in the urine of horses and other herbivorous animals. It is derived from phenyl-acetic acid, a body that can arise from the intestinal putrefaction of albumin. It usually occurs together with hippuric acid, and can be separated from the latter, as shown above, by treating the mixture with petroleum ether. The acid crystallizes in rhombic plates with rounded angles. It is decomposed into phenyl-acetic acid and glycocoll by boiling with concentrated HCl. It assumes a red color when heated above its melting point (143° C.), and emits an aromatic odor.

Other Compound Glycocolls. In addition to hippuric and phenaceturic acid a number of other compound glycocolls have been found in the urine after the administration of certain drugs and chemicals that belong to the group of aromatic organic compounds. Thus salicylic acid appears in the urine as salicyluric acid, nitrobenzoic acid appears as nitrohippuric acid, furfurol appears as furfuracryluric acid, and p-toluylic acid as toluric acid, etc. Clinically these bodies are not very important, but chemically this synthesis to glycocoll compounds is very interesting.

Aromatic Oxyacids.—To this group belong para-oxyphenyl acetic acid, para-oxyphenyl-propionic acid, two bodies that are constantly present in human urine and that are derived from the intestinal putrefaction of albumin, or possibly, too, from proteid disassimilation in the tissues. A litre of normal human urine contains from 0.01 to 0.02 gm. of these acids. In acute phosphorus poisoning and after the administration of phenol or of tyrosin the urine may contain eight times as much as the normal quantity. These oxyacids either appear in the urine as such or as conjugate sulphates.

The clinical importance of these two oxyacids is so subordinate that their properties and the methods for isolating and identifying them will not be given in this article (see Huppert, "Harnanalyse," p. 237 *ff*.).

Other members of this group are para-oxyphenyl-lactoic and oxyamygdalic acid that may both appear after feeding tyrosin or in acute yellow atrophy of the liver where much tyrosin and leucin are thrown into the circulation. All the acids enumerated may, in fact, be considered (chemically) as derivatives of tyrosin.

The two members of this group that are clinically most interesting and most important are dioxyphenyl-acetic acid (*homogentisinic acid*) and trioxyphenyl-propionic acid (*uroleucinic acid*); the two are known by the name of *alkaptonic acids*.

The Alkaptonic Acids. Alkaptonuria.—Alkaptonic acids in solution turn dark on standing. This is also the most striking feature of alkaptonuric urine. Alkaptonuria is commonly believed to indicate abnormal intestinal putrefaction. It is possible that an abnormally large amount of tyrosin is formed that after absorption leads to the formation and excretion of alkaptonic acids. Feeding with tyrosin, as a matter of fact, leads to the excretion of hæmogentisinic acid. Alkaptonuria occasionally appears in several members of a family. Such individuals may be considered chemical (*scil.* metabolic) "sports." Alkaptonuria may persist for a lifetime without any disturbance of the individual's health. It may also appear in certain diseases that are accompanied by intestinal derangement. The excretion of alkaptonic acids is always greater on a meat diet than on a vegetable diet. Antifermentative drugs and laxatives exercise no effect on its excretion.

The alkaptonic acids reduce copper and silver salts, but they do not ferment with yeast, nor are they optically active. They both give a lemon-yellow precipitate with Millon's reagent (see above under Albumin) in the cold that gradually turns orange and, on heating, becomes brick-red.

Homogentisinic Acid. The separation of the two acids is clinically unimportant, for the recognition of alkaptonuria from the above urinary characteristics is sufficient for all purposes. The recognition of pyrocatechin and hydroquinone, that may also cause darkening of the urine, has already been discussed. The presence of these bodies should be ruled out.

For completeness sake, however, the following method for isolating the alkaptonic acids from the urine and for separating the two may be given:

To 1 litre of urine 150 c.c. of twelve-per-cent. H_2SO_4 are added and the mixture extracted with ether by repeatedly shaking it with renewed quantities. In this way nearly all the alkaptonic acids can be extracted. It is a good plan to concentrate the urine before extracting with ether, care being taken that the urine is acid while evaporating. The ether is driven off, the residue, which becomes crystalline on cooling, dissolved in a large volume of water, the solution heated almost to the boiling point and treated with a concentrated solution of lead acetate. The precipitate that forms is filtered off at once and the filtrate allowed to cool. From this solution the lead salt of homogentisinic acid crystallizes within twenty-four hours in the form of large prismatic crystals. In order to manufacture the free acid the lead salt is disassociated with a stream of sulphureted hydrogen, the lead sulphide filtered off, the filtrate freed from H_2S by heating, and concentrated on the water-bath until it begins to assume a dark color. The concentration is then continued *in vacuo* over H_2SO_4. The acid crystallizes in large crystals of characteristic shape that give off 9.08 per cent. of their weight at 100° and melt at 146.5° to 147° C. They are almost insoluble in chloroform, benzol, and toluol. Their watery solution gives the above-named reactions for alkaptonic acid, and turns blue with a few drops of ferric chloride.

Uroleucinic acid has been found only in one case of alkaptonuria. It can be differentiated from homogentisinic acid by the ferric chloride reaction, for whereas the solution of the former turns blue on addition of ferric chloride, the solution of the latter turns green. Its melting point is at 190° to 193° C. It gives the reactions common to the alkaptonic acids.

Fatty Acids.—*Volatile Fatty Acids.*—Normal urine always contains traces of volatile fatty acids, chiefly *formic*, *acetic*, *propionic*, and *butyric* acids. According to different estimations, from 0.04 to 0.06 gm. of volatile fatty acids are excreted in twenty-four hours. In febrile states this quantity is increased (0.17 gm.—chiefly acetic). When the urine undergoes ammoniacal decomposition, large quantities of these acids are formed, the source of these volatile acids in this case being the carbohydrates of the urine. Of other acids of the fatty series, both volatile and non-volatile, *valerianic* acid has been found in typhoid, variola, and acute atrophy of the liver. (In these states this acid is probably a putrefaction product of leucin.) In hæmatoporphyrinuria, and in a case of phosphorus poisoning, *oleic* acid and *solid fatty acids* (melting point 49° to 51° C.) have been recovered from the urine. In diabetic urine acetic, butyric, formic, and propionic acids have been found by different investigators. In the urine of various herbivorous animals particularly large quantities of this group of acids have been found. The bulk of the volatile fatty acids excreted in the urine is unquestionably derived from carbohydrate fermentation in the intestine. A portion may also be derived from the putrefaction of albumins in the bowel or from abnormal degradation of the tissue albumins.

Isolation and Identification. The urine (preferably large quantities) is acidified with phosphoric or sulphuric acid and distilled in a current of steam. The acid that is added converts the urea into carbonate of ammonia

and is bound by the latter. The distillation is continued as long as the distillate remains acid. The distillate is then neutralized with soda, evaporated to dryness, and the residue repeatedly extracted with absolute alcohol. The alcoholic solution contains sodium salts of the fatty acids, sodium benzoate, and traces of paracresol. The benzoic acid can be removed by treating the residue obtained from the evaporation of the alcoholic extract with sulphuric acid in the cold, removing the precipitate by filtration and allowing the filtrate to stand in the cold until all the benzoic acid is precipitated. The filtrate is again neutralized with soda and shaken with ether. This removes the paracresol. The ether is removed in a separating funnel, the watery residue heated to drive off the last traces of ether, and the analysis for fatty acids undertaken in the watery solution that remains behind.

For the identification of the different acids of this group I refer to text-books of organic chemistry. The total quantity of the fatty acids present in a stated quantity of urine can be determined by preparing the distillate as above, removing benzoic acid and paracresol as indicated, precipitating the watery solution of the fatty acids with barium hydrate, evaporating to dryness, weighing the residue of barium salts of the fatty acid, redissolving in water, determining the barium by precipitation with sulphuric acid, incinerating the barium sulphate and extracting the residue with hydrochloric acid and subtracting the weight of the barium from the weight of the barium salts of the fatty acids.

Lactic Acid (*Sarcolactic, paralactic, dextrorotary lactic acid*).—Lactic acid has been found in the urine in dyspnœa, in perversions of the liver function, after excessive muscular exercise and in certain affections of the muscles accompanied by disturbances of muscular nutrition (trichinosis), and finally in certain forms of poisoning. Normal urine never contains lactic acid. Paralactic acid in the form of its ammonia salt is probably a normal constituent of the blood entering the liver. In this organ it is converted into urea. Hence it appears in the urine when the urea-forming function of the liver is impaired, as in destruction of the liver parenchyma (phosphorus poisoning, acute yellow atrophy), and in asphyxia or carbon-monoxide poisoning when the available supply of oxygen is reduced. After epileptic seizures lactic acid has been found in the urine. Here its appearance may be explained either by the increased muscular catabolism incident to the spasm or by asphyxia incident to the tonic contractions of the diaphragm. Whether or not lactic acid is a disassimilation product of carbohydrates (*i.e.*, whether or not glycogen [dextrose] is destroyed to CO_2 and H_2O viâ lactic acid) remains for the present undetermined. In this case, too, a perversion of glycolysis, or excessive disassimilation of glycogen with lack of oxygen, might account for the appearance of lactic acid in the urine.

Isolation and Estimation. In order to estimate the quantity of lactic acid excreted the lactate of zinc must be manufactured as follows: The urine is treated with a large excess of phosphoric acid and repeatedly extracted with ether. The ethereal extract is evaporated. The residue constitutes a syrupy liquid containing any lactic acid that may be present—also phenols, urea, and hippuric acid. By dissolving the residue in water and boiling the liquid with lead hydrate the extraneous matter can be removed. The solution is filtered hot and the lead precipitated by a stream of H_2S. The sulphide of lead is filtered off, the filtrate boiled in order to drive off the H_2S, and then boiled again with carbonate of zinc. The solution is then evaporated to a small volume and allowed to crystallize, the crystals of zinc lactate washed with a little absolute alcohol, dried in the air and weighed. They are then heated in a small porcelain crucible to 100° to 110° C., and the loss of water of crystallization determined. The paralactate of zinc contains 14.58 per cent. of water of crystallization (ordinary racemose lactate of zinc 18.16 per cent). In addition a zinc determination must be made further to identify the compound. The dried and weighed salt is treated with concentrated nitric acid in a porcelain crucible, the HNO_3 driven off by gentle heat, and the residue first evaporated to dryness and then glowed. The substance at first turns brown, and is finally converted into white zinc oxide. This is glowed to a constant weight. From the zinc oxide the amount of zinc present in the quantity of zinc lactate employed for the analysis can easily be calculated. The dried lactate of zinc contains 33.43 per cent. of ZnO or 26.84 per cent. of Zn.

β-Oxybutyric Acid, Diacetic Acid, and Acetone.—The chemical relation existing between these three substances may be illustrated by the following scheme:

$$\underset{\beta\text{-oxybutyric acid.}}{CH_3.CHOH.CH_2.COOH} + O = \underset{\text{Diacetic acid.}}{(CH_3CO).CH_2COOH}$$
$$= CO(CH_3)_2 + CO_2$$
Acetone.

The three substances may appear in the urine together. Every urine containing oxybutyric acid contains diacetic acid, and usually acetone. It is possible that in process of determination the precursors of acetone are frequently converted into the latter body so that acetone may apparently appear alone. Diacetic acid may also appear without β-oxybutyric acid, but urine containing diacetic acid always contains acetone; at least for the reason just stated acetone is always detected in the distillate. This at least is the author's experience.

The source of β-oxybutyric acid and its congeners is not positively known. The preponderance of evidence speaks for an albuminous origin, although there are some facts on record that speak for a carbohydrate or a fat origin of these bodies.

β-oxybutyric acid never occurs in normal urine. It is common in diabetic urine. It has been found in scarlatina and measles, but in no other febrile disease. It has been reported in scurvy, in cacrinoma (coma), in uræmia, and in a case of hysteria. The acid usually appears in the form of its alkali or ammonia salts—occasionally free. There is no definite relation in diabetes between the excretion of sugar, ammonia, and β-oxybutyric acid.

Tests.—β-Oxybutyric acid should be looked for only in urine that gives the ferric-chloride test for diacetic acid (see below). Every urine, however, that gives this test does not necessarily contain β-oxybutyric acid (see above). If the urine is levorotatory (after removal of dextrose in diabetic urine by fermentation), the presence of β-oxybutyric acid is still more probable.

Method of Külz. If the urine gives the above tests, it should be evaporated to a syrupy consistence (diabetic urine after fermentation), treated with an equal volume of concentrated sulphuric acid and distilled. The distillate should be collected in a test tube. Cooling is unnecessary. If β-oxybutyric acid was present, the distillate will contain α-crotonic acid, and this body should crystallize on cooling the liquid.

$$\underset{\beta\text{-Oxybutyric acid.}}{CH_3.CH(OH).CH_2.COOH} = \underset{\alpha\text{-Crotonic acid.}}{CH_3.CH = CH.COOH} + H_2O$$

The mother liquid is removed from the crystals by pressing them between filter paper. The dry crystals should have a melting point of 71° to 72° C. If the urine contains only small quantities of β-oxybutyric acid, and if consequently the distillate contains only very little α-crotonic acid, the latter may not form crystals. The distillate should then be extracted with ether, the ethereal solution separated from the water in a separating funnel and evaporated to dryness. The melting point of the residue may then be determined.

For quantitative determinations one litre of the urine is extracted with alcohol, the alcoholic extract treated with sulphuric acid and ether, the ethereal extracts evaporated, the residue dissolved in a small quantity of water, the solution precipitated with lead acetate, the lead removed by H_2SO_4, the filtrate brought to a definite volume (20 to 25 c.c.) and submitted to polarimetric analysis (Coefficient $[\alpha]_D = 20$). (See also Wolpe, *Arch. f. exp. Path. u. Pharm.*, vol. xxi., p. 138, 1886.)

Diacetic Acid.—This body is common in diabetes in malignant febrile diseases, during the eruptive stage of scarlatina and measles. It has been described in cholera, in gastric cancer, in many different digestive disorders, in inanition from starvation, and in persons living on an abundant animal diet. Diacetic acid, as shown above, often occurs together with β-oxybutyric acid and acetone. It may occur without the former, but it never occurs without the latter. As a matter of fact, normal urine always contains traces of acetone (see below).

Tests.—As diacetic acid is rapidly decomposed (within twenty-four hours at the latest), the specimens of urine should be fresh.

(1) Arnold's Test. This is the most useful clinical test, as it does not respond to acetone, nor to β-oxybutyric acid. It has the additional advantage that certain bodies (salicylic acid, antipyrin, phenols, acetates, skatoxyl sulphuric acid, thallin, etc.) that may be present in the urine and that respond to the popular iron chloride reaction, to be described presently, do not interfere with this test. The same applies to bile pigments that may be present. In order to make the color reaction more striking the urine may profitably be filtered through animal charcoal.

The reagents needed consist of a one-per-cent. solution of sodium nitrite and a solution of para-amido-acetophenone (1 gm. of para-amido-acetophenone dissolved in 100 c.c. of water is treated with HCl until the yellow solution becomes colorless); one part of the nitrite solution is mixed with two parts of the acetophenone solution. A small quantity of the urine is shaken with an equal volume of this reagent and then treated with a few drops of ammonia. An amorphous reddish-brown precipitate forms. This, however, does not alone denote the presence of diacetic acid. If the mixture, however, is treated with a large excess of concentrated hydrochloric acid (10 to 1), and if a violet-purplish color appears, the urine contains diacetic acid.

(2) The Ferric Chloride Reaction (Gerhardt's Test). The urine is treated with a ten-per-cent. solution of ferric chloride as long as a precipitate continues to form. After filtration (or without filtration) the liquid on addition of more ferric chloride should turn a Bordeaux-red. As other substances (see above) give the same reaction, the test is not quite reliable. The color produced with ferric chloride by most of these bodies can, however, be distinguished from the typical Bordeaux-red with a little practice. Salicylic acid produces a color that is more violet, the antipyretics a color that is more purple, and that, moreover, requires longer (two to three minutes) to appear. The diacetic acid color disappears very soon, whereas all the other colors remain permanently. The test may finally be modified in such a way that the diacetic acid is partially isolated from the urine by treating it with sulphuric acid until it is strongly acid and then extracting it with ether. The ethereal extract, when shaken with a small quantity of the ferric chloride solution, assumes the typical Bordeaux-red color that disappears again on boiling.

(3) Mörner's Test. The urine is treated with a little iodide of potassium and ferric-chloride solution in excess. On boiling, acetone-iodine(?) develops a substance that is very irritating to the mucous membranes. This test is as delicate as Gerhardt's test, but also ambiguous in the sense that the same reaction is obtained with urine containing acetone alone.

Quantitative Estimation. This can only be performed for diacetic acid and acetone together. See, therefore, quantitative estimation of acetone.

Acetone.—Normal urine always contains traces of acetone—usually about 0.001 gm. (7 to 10 mgm.). If the carbohydrates are withdrawn, the acetone excretion increases. In certain pathological conditions as much as 0.5 gm. of acetone may be excreted in twenty-four hours. The chief source of acetone are the tissue albumins. Increased catabolism of the body proteids and decreased oxidation lead to acetonuria. Whether or not urinary acetone is ever derived from intestinal fermentation of albumins remains undetermined. Acetonuria may occur in any of the following pathological conditions: Inanition from starvation, dyspnœa (asphyxia), poisoning with hæmolytic drugs, during narcosis, diabetes (here the amount of acetone excreted stands in no relation to the sugar—or the N-excretion); in hydrophobia, morphinism, phosphorus poisoning, many digestive disorders (autointoxications), in long-continued febrile diseases, and in eclampsia. It will be seen that acetonuria is a very common sign.

Tests. Legal's Test.—The urine may be treated with a few drops of a twenty-per-cent. solution of sodium nitroprusside and a small quantity of sodium hydrate solution. If acetone is present, the urine will turn red—this color rapidly fades; if a few drops of acetic acid are now added, the liquid becomes purple or violet-red. If no acetone is present, the liquid remains colorless even after the addition of acetic acid.

This is the only one of the acetone tests that can be performed with the urine itself. For all the other tests from 200 to 300 c.c. of urine, after the addition of a little phosphoric acid, must be distilled and the tests performed with the first 20 to 30 c.c. of the distillate that pass over.

Lieben's Iodoform Test.—A few cubic centimetres of the distillate are treated with a few drops of potassium hydrate solution and iodopotassic iodide added. If acetone is present, a yellow precipitate of iodoform will form, that consists of fine hexagonal plates and emits a characteristic odor of iodoform. This test is very delicate. Unfortunately a number of other bodies give the same test, notably alcohol and aldehydes.

Gunning has modified the test as follows in order to avoid this confusion with alcohols and aldehydes: He performs the test with an alcoholic iodine solution and ammonia. In the beginning a black precipitate of iodine-N develops that soon disappears, however, and brings the yellow crystalline deposit of iodoform to view. This test is not quite so sensitive as the original test of Lieben.

Reynolds' Test.—This test is based on the property of acetone to dissolve freshly precipitated mercuric oxide. The mercuric oxide is obtained by precipitating a solution of corrosive sublimate with an alcoholic potassium hydrate solution (yellow precipitate). Some of this mercuric oxide is added to the distillate and the mixture thoroughly shaken and filtered. The filtrate is superposed with a solution of ammonium sulphide. If acetone was present in the distillate, a black ring of mercuric sulphide will form at the plane of contact.

Quantitative Estimation. The Underlying Principle.—Acetone in alkaline solution is converted into iodoform by the action of iodopotassic iodide. The reaction proceeds in two stages that may be illustrated as follows:

$$I_2 + KOH = KOI + HI$$

(1) $CH_3.CO.CH_3 + 3KOI = CH_3.CO.CI_3 + 3KOH$
Acetone. Tri-iodine-acetone.

(2) $CH_3COCI_3 + KOH = CH_3COOK + CHI_3$
Acetate of potassium. Iodoform.

The amount of iodine consumed in this reaction is determined by titrating with sodium thiosulphate. The chemism of this reaction is complicated. I will limit myself to describing the execution of the method. An exhaustive explanation of the reaction will be found in text-books of chemistry.

Execution: The urine is distilled and the distillate must be free from phenols, ammonia, nitrous acid or formic acid, for all these bodies interfere with the titration or the formation of iodoform. The ammonia can be kept back by the addition of an acid; 2 c.c. of fifty-per-cent. acetic acid to 100 c.c. of urine do not liberate phenols (as stronger acids or more acid would do), but this amount allows a little ammonia to escape. The distillate should, therefore, be distilled a second time with 1 c.c. of twelve-per-cent. sulphuric acid. In order to prevent the passage of nitrous acid and of formic acid a little calcium carbonate is added to the urine prior to distillation.

To the second distillate is added an excess of a one-tenth normal iodine solution (12.685 gm. of iodine to 1,000 c.c.) and then drop by drop so much of a fifty-per-cent. solution of sodium hydrate that the color of the iodine disappears completely and the yellow iodoform precipitate appears. The mixture is thoroughly shaken and allowed to stand for five minutes. The liquid is now acidified with concentrated hydrochloric acid. The fluid turns brown from the iodine in excess that is liberated. This excess is titrated with a solution of sodium thiosulphate (one-tenth normal, *i.e.*, containing 24.8 gm. of the salt to 1,000 c.c. of water), using starch solution as an indicator. The starch should not be added until the liquid has become faint yellow on addition of a sufficient quantity of the thiosulphate. As soon as the mixture turns blue, the thiosulphate is slowly added drop by drop until finally the blue color disappears. Every cubic centimetre of the sodium thiosulphate solution corresponds to a cubic centimetre of the iodine solution. The number of cubic centimetres of the former employed in the titration can, therefore, be subtracted from the amount of iodine solution added to the distillate in order to give the amount of iodine consumed in the reaction. The figure obtained multiplied by 0.967 indicates the number of milligrams of acetone present in the amount of urine employed for the estimation.

Pigments.—Indican, indigo-red and skatol-red, alkaptone, pyrocatechin, hydroquinone have already been discussed. The rare or clinically unimportant pigments urochrome, uromelanin, humin bodies, uroerythrin, urorosein, urorubrohæmatin, urofuscohæmatin, and the large number of undefined urinary pigments cannot be described in this article. The following urinary pigments are important: (1) The bile pigments (and bile acids); (2) urobilin; (3) melanin; (4) hæmatin; (5) hæmatoporphyrin.

The Bile Pigments (and Bile Acids) (Choluria).—(*a*) *Bile pigments* are never found in normal urine. They appear in the urine whenever there is stasis of bile and diapedesis of bilirubin from the bile channels into the lymph spaces and blood-vessels of the liver ("hepatogenous" icterus). Thus choluria is one of the signs of occlusion or stenosis of bile ducts, impairment of the diaphragmatic excursions, thrombosis of the portal vein, etc. Some forms of choluria are due to so-called "hæmatogenous" icterus, *i.e.*, the development of bile pigments from the blood pigment of extravasations, hæmatomata, etc. The writer has shown that bile pigments can be formed outside of the liver whenever hæmoglobin undergoes disintegration in the tissues. The appearance of bile pigment in the urine by no means, therefore, always indicates an affection of the liver or of its ducts and vessels.

Urine containing bile pigment is usually yellowish or greenish-brown. The foam that forms on shaking the urine is usually yellow, even if the urine only contains very minute quantities of pigment. The only bile pigment that is found in freshly voided urine is bilirubin. The other bile pigments—viz., biliverdin, bilifuscin, and biliprasin—develop secondarily from bilirubin if the urine is allowed to stand. All the bile pigment voided in the urine may occasionally be found in the sediment. The differentiation of the different bile pigments is clinically unimportant. Of the many chemical tests for bile pigment only the two most practical ones will be described.

(1) Gmelin's Test.—A few cubic centimetres of yellow nitric acid are superposed in a test tube with an equal volume of urine. If bile pigment is present, a *green* ring will form at the plane of contact, in addition usually to a number of other multicolored zones. Only the *green* color is characteristic for bile pigment (biliverdin). The urine must be free from alcohol, as this substance also gives a bluish-green ring with nitric acid. Rosenbach has described a convenient modification of the test. A piece of filter paper is moistened with the urine to be tested and a drop of yellow nitric acid placed on the paper; a number of concentric colored rings form around the drop, and again only a green ring is characteristic for bile pigment. Large quantities of albumin in the presence of small quantities of pigment interfere with Gmelin's test; they had better, therefore, be removed. Small quantities of albumin in the presence of large quantities of pigment do not interfere.

(2) Huppert's Test for very Small Quantities of Bile Pigment.—Ten cubic centimetres of the urine are treated with lime water. The precipitate is removed by filtration and brought into a test tube containing sulphuric-acid alcohol. The suspension is acidified with a few drops of sulphuric acid and heated to boiling. If bile pigment is present, the liquid turns green. Again, the green color is important; indican may give a yellowish or reddish color, but only bile pigment gives a green tint to the alcoholic solution.

(*b*) *Bile acids* in the urine are always pathological. They usually appear together with bile pigment and possess the same clinical significance (see above). It is useless to attempt the direct demonstration of bile aids in the urine, as the most typical reaction for bile acids, viz., Pettenkofer's reaction, is given by a number of other normal ingredients of the urine. The bile acids must, therefore, first be isolated as follows: Albumin, if present, is removed by coagulation; the coagulate filtered off and the filtrate evaporated to dryness, the residue extracted with absolute alcohol, the alcoholic extract diluted with water and precipitated with basic lead acetate and ammonia, the precipitate filtered off, extracted with absolute alcohol and filtered hot. This solution contains any bile-acid salts that may be present and can be submitted to the following tests:

(1) Pettenkofer's Reaction (modified by Udranszky).—In the original Pettenkofer test cane-sugar and sulphuric acid were employed. Since it was shown that the sugar was converted into *furfurol* by the action of the sulphuric acid and that the furfurol gave rise to the typical color reaction with bile acid, Udranszky advised the use of furfurol in the first place. One cubic centimetre of the bile-acid solution is treated with one drop of a one-tenth-per-cent. solution of furfurol and slowly superposed upon 1 c.c. of concentrated sulphuric acid, care being taken by immersing the tube in cold water to prevent too great heating of the mixture. A purple color appears at the plane of contact that gradually extends upward into the superposed solution; on standing, the color turns bluish. In alcoholic solution a green fluorescence is seen. The pigment gives a typical spectrum, viz., two bands, the one near F, the other between D and E, near E.

(2) Platner's Crystals.—An attempt may be made to obtain crystals of the bile acids by evaporating the solution with soda, extracting the residue with absolute alcohol, and adding enough ether to produce a slight clouding. On standing, Platner's crystals of the sodium salts of the bile acids form. These may further be identified as above or by testing their effect on the heart of a curarized frog (retardation).

Urobilin.—Normal urine never contains urobilin. It does, however, contain the chromogen of urobilin, viz., urobilinogen, from which urobilin develops by the action of sunlight. Only very minute quantities of urobilin (urobilinogen) are found in normal urine (not more than from 20 to 130 mgm. in the quantity passed by a healthy adult in twenty-four hours). The high figure (130 mgm.) is only obtained if the urine is first allowed to stand so that all the urobilinogen it contains is converted into urobilin. Urobilin is produced in the bowel by putrefaction, *i.e.*, directly by the action of reducing bacteria on bile pigments. Consequently the excretion of urobilin is increased if intestinal putrefaction is great. It is absent from the urine of the new-born (first to third day) because the intestinal contents remain sterile for some time. It is also absent from the urine if the entrance of bile into the intestine is prevented (occlusion of the bile ducts as by carcinoma of the gall bladder or pancreas, catarrhal swelling, etc.). In these diseases, therefore, the *absence* of urobilin from the urine may be of diagnostic value. *Urobilin is increased* whenever hæmolysis occurs

(even if the bile ducts should be occluded at the same time—urobilin-icterus). I propose the name of "*hæmatogenous urobilinuria*" for this condition. Thus we find urobilinuria in many infectious diseases, particularly those forms that are accompanied by rapidly progressive anæmia, in poisoning with hæmolytic substances (potassium chlorate, mushrooms, etc.), in absorption of hemorrhagic exudates, effusions, cysts, etc.

Immediately after the removal of some biliary obturator (passage of a gall-stone, relief of catarrh, etc.) the urobilin excretion is increased—a direct result of the entrance of much bile into the bowel. Urobilin has also been found increased in pernicious anæmia, after chloroform narcosis, in a case of melanotic sarcoma (alternating with melanin), in lead colic, atrophic cirrhosis of the liver, and in certain valvular heart lesions that lead to passive congestion of the liver and pleiochromia.

Tests.—Urine containing much urobilin is usually very dark. The color is no index, however, of the amount of urobilin, for very dark urines may be colored by other ingredients, and may contain very little urobilin, whereas light urines may contain much urobilin, as the coloring properties of urobilin are slight. Sometimes the presence of urobilin can be demonstrated in the urine direct. Occasionally it may be necessary to isolate it from the urine.

To test the urine direct we have two tests, viz.:

(1) Fluorescence. The urine is treated with an excess of ammonia and a few drops of a one-per-cent. alcoholic solution of chloride of zinc. If the urine contains urobilin, a beautiful green fluorescence will appear.

(2) Spectroscopic Examination. Only such urine can be utilized for this test that does not contain too many other pigments. It is well, therefore, to treat the urine first with mercuric sulphate, to filter off the pigment precipitate, and to examine the filtrate spectroscopically. Ten cubic centimetres of the urine are treated with 5 c.c. of a solution of mercuric sulphate, made by dissolving 5 gm. of mercuric oxide in 20 c.c. of H_2SO_4 and 100 c.c. of water; the mixture is allowed to stand for five minutes, then filtered. The filtrate should show the absorption bands of mercuri-urobilin. The urine itself and extracts made from the urine show either the spectrum of urobilin itself or of acid urobilin. (For descriptions and illustrations of these different spectra I must refer to text-books of physiological chemistry.)

If the urine contains too little urobilin to give these tests positively, the urobilin should be extracted. One may use amyl alcohol, chlorform, phenol, ether, or acetic ether. Amy alcohol is the best.

Extraction with Amyl Alcohol (Nencki and Sieber). Ten to twenty cubic centimetres of the urine are treated with a few drops of hydrochloric acid and shaken with 6 to 10 c.c. of amyl alcohol. The alcoholic solution is submitted to spectroscopic analysis. It is then treated with a few drops of a one-per-cent. solution of zinc chloride in ammonia-alcohol. In the presence of urobilin a green fluorescence appears.

Melanin (Syn. *Phymatorhusin*).—Patients with melanotic neoplasm occasionally void urine that turns dark on standing. The dark color can frequently be brought about more rapidly by the addition to the urine of oxidizing agents, as nitric acid, chromic acid, ferric chloride, bromine, etc. The dark color may occasionally be made to disappear again if the urine is treated with reducing agents. If the urine is kept in an air-tight vessel, darkening may be prevented. Indican and urobilinogen may lead to confusion. This error can only be ruled out by testing the urine for these two bodies. After their presence is excluded the presence of melanin can be established by the properties of melanotic urine, described above.

Hæmatin is occasionally found in the urine. It is a derivative of hæmoglobin and may be formed from the latter if bloody urine is heated, the urinary acids disintegrating the hæmoglobin into hæmatin and a proteid radical. It has also been described in a case of sulphuric-acid poisoning. The presence of hæmatin is recognized by spectroscopic examination of the urine. The spectrum of hæmatin may be confused with the spectrum of methæmoglobin; hence it is necessary to treat the urine first with ammonia and to re-examine the filtrate spectroscopically; finally to add ammonium sulphide and to examine a third time. Spectra that are characteristic for alkaline and for reduced hæmatin will successively appear on the addition of these reagents. As this body is clinically unimportant, other tests and reactions will not be included in this article.

Hæmatoporphyrin.—This pigment in very minute traces occurs in normal urine (Garrod and Saillet). In a number of cases of enteric fever, Addison's disease, exophthalmic goitre, in cirrhosis of the liver, in anæmia, in lead poisoning, rheumatism, and gout considerable quantities of hæmatoporphyrin have been found in the urine. The source of hæmatoporphyrin is obscure. It does not seem to occur regularly whenever many red blood corpuscles are destroyed. The theory that it is formed in the bowel from blood pigment has been exploded.

The most important clinical forms of hæmatoporphyrinuria occur in poisoning with sulphonal, trional, and tetronal, or after the prolonged use of these drugs. The author has reported a case of sulphonal poisoning with hæmatoporphyrinuria (together with J. Tyson) in which 1.683, 1.013, and 0.098 gm. of hæmatoporphyrin were voided on three successive days, this amount corresponding to 35.1 gm. of hæmoglobin. Here about one-seventeenth of the total hæmoglobin of the subject (computed at 600 gm.) was destroyed and appeared in the urine as hæmatoporphyrin. Salkowski in one case of sulphonal poisoning obtained 0.87 gm. of hæmatoporphyrin.

Tests and Determination.—Hæmatoporphyrin urine has a typical Burgundy-red color. On standing it may turn almost black. It is possible that such urine contains other pigments besides hæmatoporphyrin. The urine is precipitated with barium mixture (consisting of one part of saturated barium-nitrate solution and two parts of concentrated baryta water). The precipitate contains the bulk of the hæmatoporphyrin together with other pigments that may be present. The precipitate is filtered off, washed and extracted with dilute hydrochloric-acid alcohol. This extract is reddish or pink in color, fluoresces and turns darker on heating. Spectroscopically a narrow absorption band between C and D in the yellow and a second broader band between D and E between the yellow and the green will be found. If the solution is alkalinized four bands will appear, one between C and D, two between D and E, and a fourth very dark band between *b* and F, *i.e.*, between the green and the blue.

Quantitative Estimation.—One hundred cubic centimetres of the urine are rendered alkaline with a dilute soda solution and precipitated with calcium chloride, again rendered alkaline with soda and the precipitate filtered off. The dark-red precipitate is repeatedly washed with water until the filtrates are free from chlorine (no precipitate with $AgNO_3$), then washed with absolute alcohol, and finally extracted with dilute HCl-alcohol at a temperature of about 40° C. From the pink alcoholic extract the pigment can be precipitated with water after neutralization of the liquid with dilute ammonia. The flocculent precipitate is gathered on a filter, washed free from chloride, washed with alcohol and ether, desiccated *in vacuo*, dried at 115° C., and weighed. This precipitate, besides hæmatoporphyrin, contains inorganic salts. A weighed portion is therefore incinerated and the weight of the ash subtracted. The difference represents organic substance, *i.e.* hæmatoporphyrin.

Fat.—For fat in lymph cells, epithelia, casts, see section on "Urinary Sediments"; for fat concretions see section on "Urinary Concretions"; for fat in chyluria, see the article on this subject.

Cholesterin has been found in chyluria (see article on this subject). It occasionally appears in the urine of pregnant women, and it has been found in the urine of

epileptics. For cholesterin in urinary concretions and sediments see below.

Tests.—The urine is shaken with ether, the ethereal extract removed, the ether evaporated, and the residue examined microscopically for crystals of cholesterin (see Fig. 4869). If the residue contains so much fat that the cholesterin cannot crystallize or the crystals cannot be recognized, the residue is treated with alcoholic KOH, the mixture boiled, evaporated to dryness, the soaps that have been formed dissolved in water, the watery solution extracted with ether, the ether evaporated, the residue dissolved in boiling alcohol, the solution evaporated to a small volume and allowed to crystallize. Cholesterin crystals touched with concentrated sulphuric acid turn red or blue (cholesterilines).

Inosite (Hexahydro-hexoxybenzol).—This body is occasionally found in diabetes mellitus, in albuminuria, and after abundant water drinking. Pohl reports a case of diabetes mellitus in which the dextrose of the urine was gradually replaced by inosite. Inosite has been called a sugar, but it does not give the chemical reactions of any of the saccharides. It is, moreover, according to Maguenne hexahydroxybenzol. In order to demonstrate the presence of inosite it must be isolated from the urine. The best method is that of

Cooper-Lane.—The urine, after removal of any albumin it may contain, is precipitated with baryta water, filtered, and the washed filtrate treated with lead acetate until no further precipitation occurs. The lead precipitate is filtered off after twelve hours' standing, suspended in water and disassociated with H_2S. The lead-free filtrate is concentrated and treated with boiling alcohol (three to four volumes). The alcohol produces a precipitate that is removed by filtration; the filtrate is allowed to stand twenty-four hours; crystals of inosite may form. These are removed by filtration, washed with cold alcohol and identified (see below). If no crystals form, the alcoholic solution is treated with ether until the liquid becomes milky. The mixture after standing twenty-four hours precipitates fine shiny plates of inosite. The crystals give the following reactions:

(1) A few crystals are heated on a piece of platinum foil with a few drops of concentrated nitric acid and the mixture evaporated to dryness; the residue is treated with ammonia and a little $CaCl_2$ solution (to bind the excess of HNO_3) and again carefully evaporated to dryness; a bright rose color indicates the presence of inosite. One milligram of the substance gives this reaction distinctly. Carbohydrates do not give it.

(2) The water of crystallization may be determined in the crystals. At 100° C. the crystals should lose 16.67 per cent. of water.

(3) Inosite tastes sweet. It melts at 217° C. It crystallizes in clino-rhomboid crystals that are usually gathered together in rosettes.

Ptomaïns.—That urine is toxic has been known for a long time. The chief cause of this toxicity are the potassium salts the urine incorporates. After removal of the K-salts the urine, however, still remains toxic. The toxicity of the urine, moreover, is not proportionate to the quantity of K-salts it contains, and the urinary ash, finally, containing all the K-salts is not so toxic as the total urine. Bouchard and his pupils are the chief exponents of the toxicity of the urine. They have published a mass of investigations on the toxicity of the urine in health and disease. The results obtained from this work are out of all proportion to the labor expended; nothing really conclusive having so far been demonstrated. This is not the place to review this large field. It may suffice to say that a variety of organic bases, alkaloids and toxalbumins, have been found by different investigators in normal and in pathological urines.

The best method for isolating ptomaïns from the urine is that described by Brieger:

Ten to twenty litres of the urine are acidified with HCl and evaporated to a syrupy consistence; the residue is extracted with alcohol and the solution precipitated with an alcoholic solution of mercuric chloride. The precipitate is extracted with much boiling water; the mercury compounds of the ptomaïns will then be found in the solution. The mercury compounds are disassociated with H_2S, the mercuric sulphide filtered off and the filtrate evaporated to a small volume. From this liquid the bases crystallize in the form of the hydrochlorates.

Enzymes.—The urine seems normally to contain proteolytic and diastatic ferments. Of the former the most common one can digest fibrin in dilute HCl solutions. It appears, therefore, to be pepsin. Another protease is occasionally found that digests fibrin in an alkaline medium. It may be trypsin. A diastatic ferment (ptyalin) is apparently one of the constant constituents of normal urine. Rennet, too, has occasionally been found. Fat-splitting enzymes have so far not been positively demonstrated. It is probable that they would be destroyed in the bladder even if they were excreted in the kidneys and would consequently escape detection. The enzyme excretion fluctuates somewhat according to time of day, the time of eating, physical exercise, etc. So far similar fluctuations that a number of authors have described in various diseases have no clinical significance. For methods to identify the different enzmyes I refer to text-books of physiological chemistry.

Inorganic Constituents.

The inorganic constituents normally present in the urine are hydrochloric, sulphuric, phosphoric, and carbonic acids; potassium, sodium, ammonium, calcium, and magnesium. Other acids occurring in very small amounts are fluoric, silicic, nitric, and nitrous acids. In addition we sometimes find peroxide of hydrogen and sulphureted hydrogen, and, finally, of the bases, iron.

Urinary Ash.—The amount of urinary ash fluctuates from 9 to 25 gm. in the twenty-four hours' quantity; the chief fluctuations being due to variations in the sodium-chloride excretion.

Quantitative Estimation of the Urinary Ash.—In determining the total ash of a given quantity of urine, the urine after evaporation to dryness should not be directly incinerated, for the alkaline chlorides are volatile at glow temperatures; the sulphates are reduced to sulphides by carbonaceous material, and the monophosphates are decomposed (escape of phosphorus). The urine is therefore evaporated and the residue merely carbonified, not incinerated, at a low temperature; the soluble salts leached out with water, the residue dried and then incinerated, and, finally, the watery extract evaporated to dryness in the crucible containing the ash and the whole weighed. This method gives very accurate results. See also "Electric Conductivity of the Urine."

Acids.—1. *Hydrochloric Acid* (Chlorides).—The quantity of HCl in the urine is largely dependent on the ingestion of salt (NaCl). The daily excretion rarely exceeds an amount that would correspond to more than 15 gm. of NaCl. The excretion of HCl salts is greatly diminished in fasting and in pneumonia during the formation of the exudate. In nephritis, with retention of solids and in certain gastric disorders (hyperchlorhydria) the urinary chlorides are also decreased. After large meals containing much salt, during the absorption of fluid transudates, in interstitial hepatitis (?), after the administration of thyroid, after inhalation of chloroform, and in the stage of convalescence from acute nephritis, the urinary chloride excretion is increased. Hydrochloric acid appears in the urine as sodium, potassium, ammonium, calcium, and magnesium chloride. Of these salts the most important and the most abundant is the sodium salt. All these chlorides are readily soluble in water.

Tests.—The urine is treated with nitric acid and a few drops of a ten-per-cent. silver-nitrate solution. The precipitation of a cheesy sediment that is readily soluble in an excess of ammonia indicates the presence of chlorides. Other substances that react similarly are iodides, bromides, and cyanides. Their presence should, therefore, be excluded in interpreting this test.

Quantitative Estimation of the Chlorides.—1. Method of Volhard. Solutions. (1) 29.042 gm. of chemically pure silver nitrate dissolved in 1,000 c.c. of water.

(2) Concentrated solution of ferric-ammonium alum (free from chlorine!).

(3) Nitric acid of 1.200 specific gravity.

(4) Solution of ammonium-sulphocyanide. This solution should be of such a strength that 25 c.c. would correspond to 10 c.c. of the silver solution. Theoretically there should be 12.984 gm. of the salt to a litre, but as ammonium sulphocyanide is very hygroscopic, it cannot be weighed accurately. Consequently the strength of the solution must be determined by titrating against the silver solution: 6 to 7 gm. of the sulphocyanide are dissolved in 400 c.c. of water and a part poured into a burette; 10 c.c. of the silver solution diluted with 100 c.c. of water are poured into a flask treated with 4 c.c. of the nitric-acid solution, and 5 c.c. of the ferric-ammonium solution, and the whole thoroughly mixed by shaking. To the mixture so much of the sulphocyanide solution is allowed to flow from the burette that the liquid in the flask assumes a faint but permanent reddish tint. Several tests of this kind are made and the average quantity of the sulphocyanide solution required determined. If it is found, for instance, that 22 c.c. of sulphocyanide produce the end reaction (red color), then the volume of water that must be added to one litre of the sulphocyanide solution is found according to the formula: $22:25 = 1{,}000 : x$; $x = 1136.3$. In other words, in order that 25 c.c. of the sulphocyanide solution correspond to 10 c.c. of the silver-nitrate solution, 136.3 of water must be added to the sulphocyanide solution. With these four solutions the chloride determination in the urine is performed as follows: 10 c.c. of the urine are poured into a flask holding 100 c.c.; to the urine are added 50 c.c. of water, 4 c.c. of the nitric acid, and 15 c.c. of the silver-nitrate solution. The contents of the flask are agitated until the precipitate settles and the supernatant fluid becomes clear. The flask is now filled to a mark that indicates 100 c.c.; 80 c.c. of the contents are then filtered through a dry filter into a dry measuring cylinder. These 80 c.c. are poured into a flask holding about 200 c.c. and are treated with 5 c.c. of the ferric-ammonium-alum solution, and with so much of the sulphocyanide solution, prepared as above (from a burette), that a faint red hue persists. The amount of sulphocyanide solution required to bring about this end reaction is determined in a series of tests and the average taken. It is assumed that the 15 c.c. of silver-nitrate solution suffice not only to precipitate all the chlorides, but also to leave an excess of silver nitrate in solution. It is this latter excess precisely that is now determined by titration with the sulphocyanide solution. The percentage of chlorides in the urine is then calculated from the deficit, according to the following formula:

$$x = (37.5 - \tfrac{5}{4} R) \tfrac{4}{10}$$

x = Amount of sodium chloride contained in one litre of urine (expressed in grams).

R = Number of cubic centimetres of the sulphocyanide solution required to bring about the end reaction.

The rationale of this formula is the following: 10 c.c. of the silver-nitrate solution correspond to 25 c.c. of the sulphocyanide solution, and 15 c.c. of the silver-nitrate solution consequently correspond to 37.5 c.c. of the sulphocyanide solution. For 100 c.c. of the test solution 37.5 c.c. of the sulphocyanide solution less $\frac{5}{4}$ of the amount of sulphocyanide solution used were needed, for 80 c.c. correspond to the amount of sulphocyanide solution taken from the burette, so that 100 c.c. would have required $\frac{5}{4}$ of this amount. As 25 c.c. of the sulphocyanide solution correspond to 10 c.c. of the silver solution, 1 c.c. of the former solution corresponds to 0.4 c.c. of the latter; and as 1 c.c. of silver solution indicates 0.01 gm. of sodium chloride (the silver solution used as a reagent is prepared in this proportion), 0.4 c.c. of the silver solution correspond to 0.004 gm. of sodium chloride. Hence in order to obtain the amount of chlorides present in 10 c.c. of urine the figure $(37.5 - \frac{5}{4} R)$ must be multiplied by 0.004. In order to determine the chlorides in one litre (1,000 c.c.) of urine the above figure must be multiplied by $0.4 = \frac{4}{10}$. (von Jaksch.)

The presence of albumin and sugar in the urine does not interfere with the accuracy of this method. It is the most accurate and the most convenient one for clinical purposes. All other methods, *i.e.*, the methods of Mohr, of Gay Lussac, of Zuelzer, are based on the same principle, viz., the titration of the chlorine with a solution of silver nitrate. As they have no advantages over Volhard's method, they will not be described in this place. A description will be found in Huppert, "Analyse des Harns," 1898, p. 705 *ff.*

Hydrofluoric Acid.—The urine contains traces of hydrofluoric acid (salts). It is clinically without any importance.

Test (Berzelius).—A large volume of urine is precipitated with ammonia, the precipitate calcined, treated with an equal volume of H_2SO_4 and heated in a platinum crucible. Over the crucible a glass plate is held. If HFl is present, it will etch the glass.

Sulphuric Acid (Sulphates).—Sulphates occur in the urine as mineral (preformed) and conjugate sulphates. For the latter see the chapter on Conjugate Sulphates above. The total SO_3 excretion fluctuates from 1.5 to 3 gm. in twenty-four hours on a mixed diet. The chief source of the sulphates are the albumins; the greater, therefore, the percentage of proteid pabulum, the greater the sulphate excretion. The conjugate sulphates constitute about one-tenth of the total sulphates. In certain pathological conditions the excretion of conjugate (ethereal) sulphates is greatly increased (see above), so that this proportion is changed in favor of the conjugate sulphates. In addition to preformed and conjugate sulphates the urine also contains sulphur in the form of sulphocyanides, thiosulphates, and sulphureted hydrogen, so-called "neutral sulphur" (see below).

The preformed sulphates of the urine are the sodium, potassium, magnesium, and calcium sulphate. The absolute increase or decrease of the preformed sulphates is of slight clinical significance. It is important, however, as pointed out above, to determine the relative proportion of preformed and conjugate sulphates; hence the quantitative estimation of the preformed sulphates is often necessary.

Qualitative Determination of Preformed Sulphates.—The urine is acidified with acetic acid and treated with barium chloride. A white, fine, powdery precipitate indicates the presence of preformed sulphates. This reaction is always obtained in normal urine. If the urine is not rendered sufficiently acid, the barium chloride may also precipitate phosphates or oxalates (or even uric acid). In order to differentiate the sulphates from these other bodies the precipitate is warmed with dilute HCl. This leads to the solution of oxalates and phosphates and leaves the sulphates behind.

Quantitative Determination of Preformed Sulphates. The preformed sulphates can either be determined directly or the total sulphates and the conjugate sulphates can be determined separately and the preformed sulphates calculated from the difference.

Total Sulphates.—The urine is treated with concentrated HCl and heated to boiling. This decomposes the conjugate sulphates into aromatic constituents and sulphuric acid. In the liquid the sulphates are precipitated with barium chloride, filtered off, and determined as barium sulphate.

Fifty cubic centimetres of urine are diluted one-half and treated with 5 to 10 c.c. of strong HCl heated to boiling and precipitated with a slight excess of barium chloride. The mixture is allowed to stand for twenty-four hours in the cold and filtered; the precipitate is washed with hot water, alcohol, and ether, and dried. The filter is then incinerated and weighed. One hundred parts of barium sulphate correspond to 34.28 parts of SO_3, or 41.13 parts of SO_4, or 41.99 parts of H_2SO_4, and the result may, therefore, be expressed as SO_3, or

SO_4, or H_2SO_4 by multiplying the weight of the barium sulphate by 0.3428, 0.4113, or 0.4199.

Determination of Conjugate Sulphates (Baumann).—The preformed sulphates are precipitated by barium chloride in the urine after it has been acidified by acetic acid. In the filtrate the conjugate sulphates are then determined.

Fifty cubic centimetres of urine are rendered acid with acetic acid, diluted one-half and precipitated with barium chloride in excess, heated on the water-bath until the barium sulphate settles at the bottom of the vessel, and filtered. The filtrate and washings are then treated as above, *i.e.*, the conjugate sulphates decomposed with HCl and the liberated sulphate determined as barium sulphate. By subtracting the value obtained for conjugate sulphates from the value obtained from the determination of the total sulphates the amount of preformed sulphates can be estimated.

Determination of Preformed Sulphates Directly.—As the barium sulphate precipitate obtained from the original urine often contains phosphates and oxalates, it cannot be weighed directly. In order to get rid of these impurities the precipitate must be repeatedly treated with HCl in a platinum crucible. The procedure is very tedious and is superfluous in view of the fact that the preformed sulphates can be estimated from the difference between total and conjugate sulphates with less trouble. They can also be determined directly by *titration* as follows:

Method of Freund.—Fifty cubic centimetres of urine are treated with ten drops of alizarin red. This colors the urine red. Then five-per-cent. acetic acid is added drop by drop until the red color disappears. When this point is reached, 5 c.c. more of acetic acid are added. The urine is then heated almost to boiling and barium acetate solution added until the liquid again turns red. The solutions required for this estimation are:

(1) A solution of 9.579 gm. of anhydrous barium acetate in 1,000 c.c. of water; 24 c.c. of this solution should correspond to 0.2101 gm. of $BaSO_4$.

(2) Five-per-cent. acetic acid.

(3) One-per-cent. solution of sodium alizarin monosulphate ("alizarin red").

As it is known that 24 c.c. of the barium solution correspond to 0.2101 gm. of $BaSO_4$, the calculation of the preformed sulphates in the 50 c.c. of urine employed in the analysis is simple.

The "Neutral Sulphur" (synonym: suboxidized sulphur, organic sulphur).—Some twelve to fifteen per cent. of the total sulphur of the urine consists of a number of bodies of which we know relatively little; among them are thiosulphates, sulphocyanides, and derivatives of taurin and cystin. A portion of these bodies is readily oxidized, whereas another portion is not oxidized so easily; the former can therefore be converted into sulphuric acid by chlorine or bromine water, the latter require fusing with nitre and potassium hydrate. Cystin belongs to the last-named group of bodies, also taurin, whereas the thiosulphates and rhodanates (sulphocyanides) belong to the former group. The quantity of neutral sulphur compounds is dependent on the quantity and the character of the albumins that are disintegrated in the organism. The neutral sulphur is increased after violent muscular exercise, after a long period of starving, in asphyxia, in chloroform narcosis, after the administration of chloral and of sodium carbonate and sodium citrate (Jawein). After the ingestion of sublimed sulphur a portion of this sulphur reappears in the urine as neutral sulphur. In icterus the neutral sulphur is increased from four to five times above normal (sixty-two per cent., Lépine). In pneumonia the neutral sulphur has also been found increased. In hepatic disorders the compounds that are hard to oxidize seem to be increased, whereas in pneumonia the compounds that are readily oxidizable are increased.

In *cystinuria* a peculiar urinary anomaly characterized by the excretion of cystin, the excretion of neutral sulphur is greatly increased (23.4 to 45.7 per cent.). In addition to cystin certain diamins (putrescin, cadaverin) are found in the urine, and as the disease seems to occur in families, and may persist for a lifetime, we are probably dealing with a peculiar metabolic anomaly in which the oxidation of the albumins is perverted. Some authors (v. Jaksch) are inclined to attribute cystinuria to a particular form of intestinal mycosis. I consider the former view more plausible. The disease is very rare. The chief clinical significance of the urinary excretion of cystin is the tendency to calculus formation that is thereby created. The appearance of cystin in the urine should always constitute a warning of impending cystin gravel or calculi. (See also Urinary Sediments.)

Tests for Neutral Sulphur.—The total sulphuric acid is first precipitated by hydrochloric acid and barium chloride, as explained above, the excess of barium removed from the filtrate by soda, the filtrate evaporated to dryness, the residue fused with nitre (and soda), the solution of this fused mixture treated with barium chloride, and the sulphuric acid precipitated. To determine the presence of sulphur that is readily oxidized the filtrate of the urine after removal of the total sulphuric acid, as above, is acidulated and treated with bromine; on addition of barium chloride any sulphuric acid formed by this mild oxidation will be precipitated.

The qualitative tests for thiosulphates and sulphocyanides will not be given in this article, because the clinical significance of these bodies is too subordinate.

The quantitative estimation of the neutral sulphur is performed according to the same principles as the qualitative tests for this group of bodies. The urine may first be oxidized and the total sulphur determined; then the total performed and conjugate sulphates may be determined separately and the quantity of the neutral sulphur calculated from the difference. In order to determine the total sulphur by oxidation a measured quantity of the urine is evaporated to dryness and the residue glowed with a fusing mixture consisting of four parts of nitre and one part of soda. The white ash is treated with hydrochloric acid and evaporated to dryness, this process being repeated three or four times in order to get rid of all the nitric acid. The residue is then dissolved in water and the sulphuric acid determined as described above. Other methods of oxidation, *i.e.*, with nitric acid (Mohr), with sodium superoxide (Clark), will not be described, as they possess no advantages over the oxidation with nitre soda.

Cystin may be precipitated from the urine by benzoyl chloride, and the sulphur determined in the precipitate. Two hundred cubic centimetres of the urine are treated with 10 c.c. of benzoyl chloride and 70 c.c. of a ten-per-cent. sodium hydrate solution and shaken until the odor of benzoyl chloride disappears. The precipitate consists of benzoyl cystin and can be used directly for a sulphur determination by oxidation. The presence of cystin in the benzoyl chloride precipitate is made probable if a black sediment forms when the precipitate is boiled with a solution of lead oxide in soda lye. The black sediment consists of lead sulphide, and consequently also denotes the presence of sulphur.

Sulphureted Hydrogen.—Sulphur may finally occur in the form of sulphureted hydrogen. Fresh urine rarely contains H_2S or sulphides, but nearly every old urine emits an odor of H_2S when treated with mineral acids. Hydrogen sulphide does not appear in the urine in diseases that are accompanied by putrefactive processes, nor does it appear after the ingestion of alkali sulphides, nor after sulphur baths. Occasionally H_2S passes into the bladder from the rectum if some abnormal communication exists between these two viscera. Certain bacteria may infect the bladder and may lead to the generation of H_2S in this viscus.

Tests.—The urine should of course be fresh. The *odor* may be characteristic. Lead acetate may form a black precipitate of lead sulphide. A piece of paper may be saturated with a solution of lead acetate, the urine poured into a bottle, and a current of air forced through the liquid. The lead paper is held over the neck of the bottle. If H_2S is driven off, the paper will turn brown

or black. Quantitative determinations of H_2S in urine are clinically without value.

Phosphoric Acid (*Phosphates*).—The urine always contains phosphoric acid; the average daily excretion is 3.5 gm. of P_2O_5; the quantity is largely dependent on the character of the diet; increased catabolism of cell nuclein either of the food or of the proper tissues causes an increase of phosphoric acid.

Four phosphates appear in the urine, viz.: (1) NaH_2PO_4 = monosodium phosphate; (2) Na_2HPO_4 = disodium phosphate; (3) Na_3PO_4 = trisodium phosphate; (4) Na_3PO_4 (+NaOH) = basic sodium phosphate. (1), (2), and (3) are also called the acid, neutral, and basic phosphate respectively; (4) would then be "overbasic." Some writers speak of (1), (2), and (3) as primary, secondary, and tertiary phosphate. The designation adopted above is the most popular and the most rational one.

The monophosphates can be converted into the di- and triphosphates by the addition to the urine of alkali hydrates or carbonates. Inversely the tri- and diphosphates can be converted into monophosphates by acids.

Tests. In acid urine the addition of ammonia at once produces a precipitate of earthy phosphates. The filtrate contains normal alkali phosphate. The latter when treated with magnesia mixture gives a precipitate of triple phosphate; or the filtrate may be acidulated with acetic acid and tested for phosphoric acid with uranium nitrate or ferric chloride. The former produces a yellowish-white precipitate, the latter a white precipitate that stains yellow with an excess of ferric chloride solution. For the analysis of phosphatic sediments see below under Urinary Sediments.

Sometimes it is necessary to get rid of the urinary phosphates prior to undertaking certain other tests. For this purpose the urine is precipitated with neutral or basic lead acetate, or the urinary phosphates are converted into normal phosphates by treating the urine with alkali hydrate and the solution precipitated with some calcium or barium salt. The filtrate will be free from phosphates.

Quantitative Estimation. Solutions.—(1) Solution of uranium nitrate containing 35.461 gm. of the salt to a litre. Uranium nitrate is dissolved in a little less than 1,000 c.c. of water and titrated against a solution of disodium phosphate (10.0845 gm. of $Na_2HPO_4,12H_2O$ to 1 litre), 50 c.c. of which should correspond to 0.1 gm. of P_2O_5. In order to bind the nitric acid developed in this titration, 3 gm. of sodium acetate are added to the uranium nitrate solution. The results of the titration indicate how much the uranium nitrate solution must be diluted to correspond to the phosphate solution.

(2) A solution of 100 gm. of sodium acetate and 30 gm. of acetic acid to a litre, 5 c.c. of this mixture are used for every 5 c.c. of urine. The solution contains enough acetic acid to convert all the urinary phosphates into monophosphate.

(3) Tincture of cochineal to be used as an indicator, 5 gm. of cochineal are dissolved in the cold in 500 c.c. of a mixture of 4 parts of water and 1 part of alcohol. Any undissolved residue is removed by filtration.

The uranium solution is now standardized; 20 c.c. should exactly neutralize 50 c.c. of the phosphate solution; 50 c.c. of the latter solution are mixed with 5 c.c. of the acetate solution (2) and a few drops of the indicator (3) added. The mixture is heated to boiling and uranium solution added, drop by drop. The appearance and persistence of a green-colored precipitate indicates the end reaction. If in this titration only 18 c.c. of uranium solution were required to neutralize the 50 c.c. of phosphate, then the uranium nitrate solution must be diluted so that 2 c.c. of water are added to every 18 c.c. of the solution.

Execution: Fifty cubic centimetres of urine are treated exactly as the 50 c.c. of phosphate solution above. As 20 c.c. of the uranium nitrate solution correspond to 50 c.c. of the phosphate solution, and as these 50 c.c. represent exactly 0.1 gm. of P_2O_5, the phosphate content of the urine can be estimated by simple calculation from the number of cubic centimetres of the uranium solution required to bring about the end reaction in 50 c.c. of urine.

The separate estimation of the different phosphates cannot be discussed in this place. (I refer to Huppert, "Harnanalyse," p. 734 *ff.*, 1898.)

Carbonic Acid (*Carbonates*).—The urine may contain free carbonic-acid gas or carbonic acid combined with various bases as carbonates. Free carbonic acid can be driven off by physical means (boiling, passage of an air current, evacuation); the latter can only be removed by chemical means (acids). The proportion of the former to the latter is about as two to one. Normal urine of the specific gravity of 1.020 and of acid reaction on an average contains about 50 c.c. of free carbonic acid; urine of an alkaline reaction over 100 c.c. of carbonic acid. As the salts of vegetable acids appear in the urine as carbonates, a vegetable diet (citrates, acetates, tartrates, etc.) leads to an increased excretion of carbonates.

An important interrelationship exists between the free CO_2, the carbonates, and the phosphates of the urine. Monosodium phosphate liberates CO_2 from alkali carbonates. If the free CO_2 developed in this way is removed, more alkali carbonate is disassociated until finally only traces of it are left. Carbonic acid forms mono- (acid) and di- (normal) carbonates ($NaHCO_3$ and Na_2CO_3). The urine may contain the carbonates of Ca, Mg, and NH_3.

Tests. A current of air is passed through an alkali hydrate solution (to remove any CO_2 it may contain), then through the urine, and finally through a solution of barium hydrate (baryta water). The presence of CO_2 will be revealed by clouding of the barium solution. Fixed alkali carbonates must first be disassociated by treating the urine with mineral acids.

Quantitative Estimation. This is performed in the same way as the qualitative test. The vessel containing the baryta solution is weighed before and after; the difference represents the CO_2 absorbed. For details I refer to text-books of analytical chemistry.

Silicic Acid (*Silicates*), *Nitrates* and *Nitrites*, and *Hydrogen Peroxide* are all occasionally encountered in traces in human urine. The silicates, nitrates, and nitrites are derived from the ingesta, probably from drinking water that always contains all these bodies. The source and significance of the traces of H_2O_2 that are occasionally found are not understood. None of these substances have sufficient clinical importance to warrant a description of their properties, nor of the methods employed for their detection and estimation in the urine.

Bases.—The bases normally occurring in the urine have been in part discussed under the headings of chlorides, sulphates, phosphates, etc. For the exact quantitative determinations of K, Na, Ca, Mg, and Fe, that are of great scientific interest in metabolic work, but only of subordinate, practical, *i.e.*, clinical interest, I refer to text-books of quantitative chemical analysis. The quantitative determination of *ammonia* alone is of sufficient practical importance, however, to warrant description in this article (see below).

The bases of the urine can be conveniently discussed in groups (Na and K, Ca and Mg, NH_3, Fe). The facts given under acids (and salts) may be supplemented by the following information:

Potassium and Sodium.—The urine voided in twenty-four hours by a healthy adult contains from 2 to 4 gm. of potassium (K_2O) and from 4 to 8 gm. of sodium (Na_2O). The excretion of Na and K is largely dependent on the character of the diet. During inanition their quantity is reduced and more K is excreted than N. As soon as food is taken, the excretion increases only slowly and the normal proportion between Na and K is soon reestablished. Vegetable K salts increase the Na excretion. Muscular exercise increases the K excretion. In fever the K excretion may be doubled or trebled and the Na excretion be greatly reduced. As soon as the fever disappears the Na excretion rises and the K excretion falls (Salkowski). These peculiar fluctuations may, I think, in large part be explained by the small ingestion of

food (containing NaCl) during fever and the increased feeding during convalescence.

Tests. Sodium.—The urine is evaporated to dryness. The residue held in a colorless flame colors it yellow. Spectroscopically an absorption line at D.

Potassium.—One hundred cubic centimetres of urine are acidified with HCl, and treated with a mixture of equal parts of alcohol and ether containing platinum chloride. In the course of three to four hours octahedric crystals of K platinum chloride from a yellow precipitate that presents characteristic microscopic features.

Calcium and Magnesium.—The average daily excretion of Ca(CaO) is from 0.2 to 0.3 gm., of Mg(MgO) from 0.1 to 0.25. Only a small proportion of the Ca absorbed from the intestine is excreted in the urine (five to fifteen per cent.); the greater portion passes into the bowel. Abundant water drinking increases the urinary Ca excretion. During inanition there is a slight increase in the Ca excretion (probably derived from osseous tissues). In osteomalacia the Ca excretion is increased; in rachitis it is not increased. The writer has shown that in tuberculosis the Ca excretion is often increased.

Tests. If the urine is treated with ammonia the precipitate that forms consists largely of Ca phosphate and Am-Mg phosphate. In order to demonstrate the presence separately of Ca and Mg the precipitate (or the sediment of alkaline urine) is dissolved in acetic acid, the solution treated with ammonium chloride and a solution of ammonium oxalate. The Ca is precipitated as Ca oxalate, while Mg remains in solution. By adding ammonia to the filtrate, Mg can again be precipitated as Am-Mg phosphate.

Ammonia.—The normal daily excretion of Am is from 0.3 to 1.2 gm. The urinary Am constitutes from 4.5 to 7 per cent. of the total N. On an abundant meat diet more Am is excreted than on a vegetable diet. As urine readily undergoes ammoniacal fermentation the urine should be examined fresh. Fixed alkalies and vegetable alkalies (that are excreted as carbonates) decrease the Am excretion, inorganic alkali salts increase it. Ammonia salts (carbonate and vegetable salts) appear in the urine as urea. As urea is formed from Am carbonate in the liver, the Am excretion (both absolutely and in proportion to urea) is increased in advanced affections of the liver (interstitial hepatitis, etc.). In amyloid liver and in splenic leukæmia the Am excretion is increased. Inorganic acids lead to an increased excretion of Am. Acidosis of the blood from whatever cause also increases the urinary Am. Asphyxia, febrile conditions with high temperatures, diabetes, phosphorus poisoning—all lead to an increased Am excretion, and this phenomenon can readily be explained either on the basis of acidosis or impairment of the liver function. Excessive Am excretion has been observed in the algid stage of cholera (2.075 [!] Rumpf).

Qualitative Test. As urea is readily converted into Am carbonate by micro-organisms the urine must be quite fresh. The urine is rendered alkaline with lime water. Am escapes and colors red litmus paper blue. KOH and NaOH cannot be used in this test because they may liberate Am from other nitrogenous bodies of the urine than Am salts. The precipitate of K platinum chloride described under Potassium may be treated with NaOH; it will also emit vapors of Am that can be recognized as above.

Quantitative Tests. The most popular method is that of Schlösing; it is not quite accurate and it has frequently been modified in minor details. The original method is, however, so simple of execution, and requires so little paraphernalia, that it is best suited for clinical work. The methods of Wurster (distillation), of Heintz, and of Schmiedeberg (determination as Am platinum chloride) are all good. I refer to Huppert, "Harnanalyse," 1898, p. 743 *ff.*, for details.

The Method of Schlösing. Twenty-five cubic centimetres of filtered urine are poured into a shallow crystallizing dish; upon this is placed a metal triangle that serves to support a second flat dish containing 20 c.c. of one-fourth normal H_2SO_4. To the urine are added 10 c.c. of lime water. The two vessels are at once covered with a bell jar with ground edge that is greased; it is pressed tightly down upon a ground glass plate. After three or four days all the ammonia is driven out of the urine and is absorbed by the sulphuric acid. The acid is then titrated back with one-tenth normal sodium hydrate solution, using methyl orange as an indicator. The ammonia absorbed by the acid, *i.e.*, originally contained in the urine, can readily be calculated from the number of cubic centimetres of the alkaline solution required to neutralize the free acid remaining. (The number of cubic centimetres of one-tenth normal NaOH may be subtracted from 50 and multiplied by 1.7 to indicate the milligrams of NH_3 found).

Iron.—Iron occurs in the urine only in organic combinations; hence its presence can only be demonstrated in the urinary ash. The uric-acid crystals of the urine usually contain some of the iron. The color of the uric-acid crystals is not, however, due to the traces of iron they may incorporate. The nature of the organic iron compound of the urine is not known. The average daily iron excretion is about 4 mgm. In fever and in pernicious anæmia the urinary iron is increased.

Test. The urinary ash is dissolved in a little HCl and boiled with one drop of nitric acid. After cooling the liquid is treated with potassium sulphocyanide solution. If iron is present even in traces a few drops of this reagent will produce a reddish color; if much iron is present, the liquid will turn dark red. Or the HCl-HNO_3 solution of the ash may be treated with potassium ferrocyanide solution. If iron is present, a blue flocculent precipitate will form.

Accidental Admixtures.—Many drugs and poisons may occasionally appear in the urine. See for this subject the article on *Poisons*.

URINARY SEDIMENTS.

The urine is usually quite clear or only slightly clouded when fresh. On standing, a small nubecula soon forms that, on microscopic examination, is found to consist of a small number of epithelial cells, a few leucocytes, and a scanty number of crystals. The size and the density of this nubecula varies greatly even in health. If the urine is concentrated, large urate precipitates may form in subjects who are perfectly well. Pathologically, many other organized and unorganized morphotic elements may appear in the urine that have great diagnostic significance. Pathologic urines containing many abnormal elements usually precipitate a distinct sediment after standing a short time. In other cases the pathologic constituents may be so scanty that they must be precipitated by centrifugation. If it is desired to preserve the sediment for a time the urine should be treated with chloroform water (5 c.c. to 1 litre). Staining the sediment is rarely necessary. The same methods and the same stains may be used as in other histologic work.

Organized Sediments.

Red Blood Corpuscles.—These elements appear in the urine in extrarenal and renal hæmaturia (see these paragraphs). The cells appear under the microscope as yellow circular discs with a central depression; seen from the side they assume a biscuit form. They soon undergo morphologic changes, and either swell up or shrink and lose their circular contour. They also appear together with white blood corpuscles and can be distinguished from the latter by the absence of a nucleus, their yellowish col-

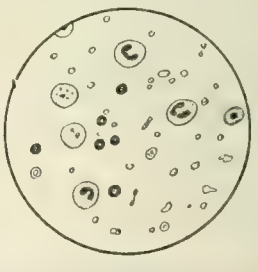


Fig. 4857. Red and White Blood Corpuscles.

or, the central depression, and their size. (See Figs. 4857 and 4858 *b* and *c*). There are always more red than white cells in simple hæmaturia; in pyuria there are more white than red. Occasionally the pigment is washed out of the red blood corpuscles, and they appear as rings ("shadows").

White Blood Corpuscles (Leucocytes, Pus Cells).—A few leucocytes can always be found in normal urine. They appear as round colorless elements with one or more nuclei and with homogeneous, finely or coarsely granular protoplasm. The smaller leucocytes usually possess only one nucleus and homogeneous protoplasm (see Figs. 4857 and 4858, *b* and *c*). The finer differences can best be brought out with Ehrlich's triple stain, but for ordinary urinary diagnosis this is superfluous. Many degenerated forms are often seen, particularly in alkaline urine. The normal outline may be lost, the cells may be swollen, their protoplasm may be in all stages of fatty, hyaline, or granular degeneration. Sometimes nothing is left of the cells but the nucleus. The greatest number of leucocytes (pus cells) appears in rupture of an abscess into the urinary passages and in cystitis. The pus may be derived from any portion of the uropoietic apparatus. In renal suppuration the number of pus cells is usually small. The localization of the pus focus may occasionally be attempted from the examination of the other formed elements that appear in the urine at the same time (see *Epithelia*). Particular care should be exercised in women, as much pus may come from the genital apparatus. In order to differentiate pus cells from epithelial cells the sediment may be treated with iodic-potassium iodide. The leucocytes will turn mahogany brown (glycogen), while the epithelia will turn light yellow.

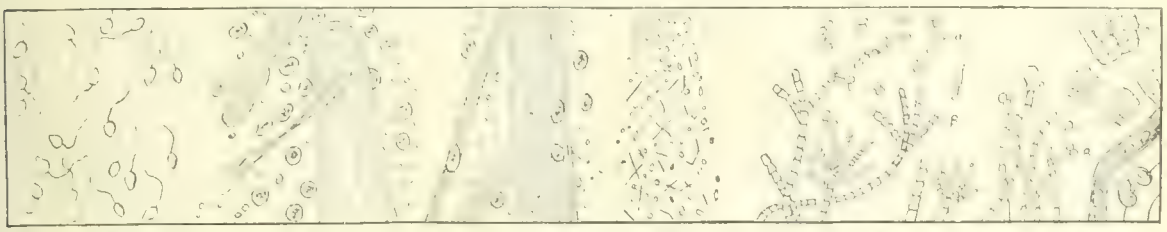


Fig. 4858. *a*, Spermatozoa; *b*, cylindroids, pus cell and white blood corpuscles; *c*, fibrin, red and white blood corpuscles, hæmaturia; *d*, micrococcus ureæ, bacillus ureæ, large bacillus found in cystitis; *e*, yeast (*a*), penicillium glaucum (*b*); *f*, oidium albicans (*a*), mycelial filaments (*b*), sarcina (*c*). Original.

Spermatozoa (Fig. 4858 *a*).—These consist of a head and a tail; the former thick and pear-shaped, the latter thin and filamentous, and becoming attenuated at its distal end. In some cases the spermatozoa are motile. They are about 50 μ long, the head usually being from 4 to 5 μ in length.

Spermatozoa are found after coitus or emissions (epileptic seizures, nocturnal pollutions, etc.) in male urine, and may also occasionally be found in the first urine voided by women after coition.

Parasites.—For pathologic bacteria and for animal parasites I refer to other portions of this work. The urine may contain almost any one of the *pathogenic bacteria*. Particularly common are the gonococcus, the tubercle bacillus, and septic cocci. Of animal parasites (vermes) distoma hematobium, filaria sanguinis hominis, echinococcus, eustrongylus gigas, and occasionally ascarides are found in the urine. Various *infusoria* have also been described in the urine. Of non-pathogenic schizomycetes and hyphomycetes and non-pathogenic bacteria (cocci, bacilli, sarcinæ, etc.) a great many have been described. The most important ones of this group are micrococcus ureæ, bacillus ureæ, a long bacillus frequently found in cystitis urine, a sarcina, yeast, penicillium glaucum, oïdium albicans, and mycelia. The appearance of some of these organisms is pictured in Fig. 4858, *d*, *e*, and *f*. Few of them are ever found in fresh urine. They rapidly develop, however, in old urine, particularly in diabetic urine, so that they may form a film or zoogloœa on the surface of the liquid. They bring about fermentative changes that have been referred to incidentally in the text above.

Epithelia are found in normal urine. Their number, however, is scanty. Occasionally normal urine contains large numbers of round epithelia that are derived from the prepuce in men or the meatus urinarius or the vagina in women. If such epithelia are present in very large number, this finding usually denotes catarrh of these parts. It is a very difficult matter to differentiate the epithelia of the kidneys, the pelvis, ureters, bladder, and urethra. As a rule, although not always, *renal epithelia* are smaller than the epithelia from lower portions of the urinary tract. They have a large oval nucleus, a polyhedric outline, and granular protoplasm. They may be single or arranged in groups. If cells possessing all the above characteristics are found arranged in cylinders (see also *Casts*) the diagnosis of renal epithelium is justified. The renal cells may be in all stages of degeneration, and occasionally a tentative diagnosis of the character of the renal epithelium may be permitted from the appearance of these cells. *Pelvis cells* are usually elongated with a thick rounded end containing a nucleus and a longer attenuated extremity (Fig. 4859, *e*). I never attach much importance to cells of this appearance, for I believe that they can be derived from the kidneys or the ureters as well, for the epithelia lining these portions of the urinary passages are after all of the same type, and any morpho-

Fig. 4859. Epithelia. *a*, Male urethra; *b*, vagina; *c*, vesical; *d*, renal; *e*, pelvis and ureter. (Original.)

logical differences that may occasionally be observed are probably accidental. Large islands of squamous epithelium speak for cystitis. In men they are in all probability derived from the bladder mucosa; in women they may be bladder or vaginal epithelia. When we consider finally that all these epithelial cells may be and usually are degenerated and consequently changed in outline and appearance, we should be warned not to place too great diagnostic importance on slight morphologic differences they may present. Fig. 4859 illustrates in a diagrammatic manner the different forms of urinary epithelia.

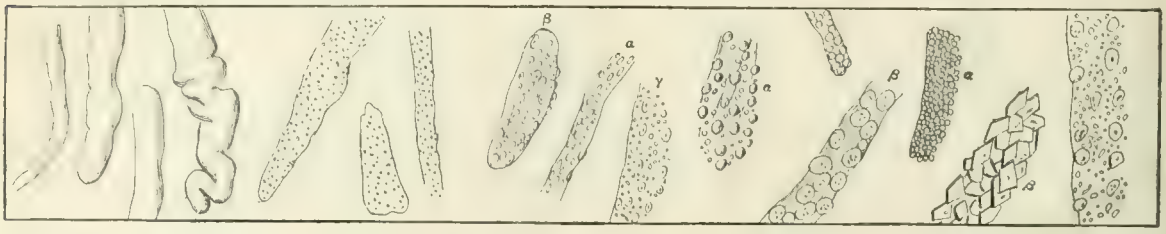


FIG. 4860. Casts. *a*, Waxy and hyaline casts; *b*, granular casts; *c*, blood casts; (α) red blood-corpuscle cast; (β) leucocyte cast; (γ) mixed blood cast; *d*, (α) fat casts; (β) epithelial cast; *e*, pseudo-casts; (α) urate cast; (β) dicalcium phosphate cast; *f*, mixed cast. (Original.)

CASTS.—Urinary casts or urinary cylinders are clinically the most important morphotic elements of the urine. We can distinguish organized casts and unorganized casts, the former consisting of morphotic elements or the products of their metamorphosis (*scil.* degeneration), the latter consisting of crystals of inorganic urinary constituents. Some writers class the latter as *pseudo-casts*, and include under the category of casts proper only the former. I consider this differentiation to be more useful from the clinical standpoint.

Casts proper may again conveniently be subdivided into homogeneous (waxy, hyaline) casts, cell casts (epithelial, blood, etc., casts), and casts consisting of formed degenerated cell products (fatty, granular, etc., casts). Often we encounter *mixed casts*, *i.e.*, for instance a homogeneous cast with cellular elements and degeneration products and frequently crystals besides. Bacterial casts are also occasionally seen. All classification of casts is more or less artificial and serves no real purpose.

Casts may appear in varying numbers. They may appear in urine that is free from albumin, or even in urine that contains no other pathologic ingredients. Normal (?) urine may contain casts. To what extent the appearance of casts is ever "physiological" it is hard to say. (See also *Physiological Albuminuria.*) Slight toxic influences (alcohol, intestinal auto-intoxication, etc.) may lead to the excretion of casts in the urine.

The appearace of the different forms of casts is illustrated in Fig. 4860.

Wavy Casts.—The origin of these casts is obscure. They may result from coalescence of degenerated epithelia, from inflammation, from exudation of amyloid or fibrin into the uriniferous tubules. They are usually long, often segmentated, sometimes short and broad (fragments). They may either be smooth or shiny, or may be covered with morphotic elements. They always indicate some renal affection. They appear in acute and chronic nephritis, in amyloid kidney, and in contracted kidney. They occasionally give the amyloid reaction, but not always. A positive amyloid reaction does not necessarily indicate amyloid kidney.

Hyaline Casts.—These structures are usually very long, pale, and very delicate, so that they may readily escape detection. Hyaline casts alone are probably of no pathologic significance, and nephritic lesions should never be diagnosed from their presence alone. Frequently they are covered with morphotic elements that possess pathologic importance.

To the same category probably belong *cylindroids* (Fig. 4860, *b*). These constitute bands and cylinders that are similar in appearance to hyaline casts. They are very common. Occasionally they are found in normal urine. They seem to be a product of slight renal irritation, but their presence by no means indicates a renal lesion proper. They have been found in congestion of the kidney, from heart lesions, and in increased urate excretion.

Blood Casts.—These structures are formed whenever there is hemorrhagic exudation into the canaliculi of the kidney parenchyma. The origin of

Epithelial Casts is equally clear. They are the result of epithelial desquamation that may be due to a great variety of causes.

The presence of blood and epithelial casts always denotes acute nephritis or an acute exacerbation of a chronic nephritis. They are consequently of the greatest diagnostic importance.

Fatty Casts.—Fat droplets are frequently found on granular casts; sometimes casts consisting of fat globules alone are seen. Occasionally fat globules and fat needles (crystals of fatty acids and soaps) appear together. Fatty casts occur only in subacute and chronic forms of nephritis that lead to fatty degeneration of renal parenchyma, *i.e.*, of renal epithelia.

Granular Casts.—These casts probably result from granular degeneration of blood and epithelial casts. They indicate renal inflammation. They occasionally appear in cyanotic induration of the kidney. They usually appear together with the other forms of casts described, and they possess great diagnostic significance.

Bacterial Casts usually indicate embolic septic nephritic processes. They often resemble granular casts in appearance, but can usually be distinguished from the latter by their resistance to nitric acid, potassium hydrate, and other strong chemicals.

Pseudo-Casts.—To this class belong hæmatoidin casts, "detritus casts," and casts holding crystals of urates, sulphates, etc. They are common in the new-born and in nephritis uratica. Their clinical significance is very slight.

UNORGANIZED SEDIMENTS.

The character of the inorganic sediment is dependent on the reaction and the concentration of the urine and on the mixture of salts it contains. Much can be elicited in regard to the sediment from its behavior to heat, the reaction of the urine and its behavior to acids. Thus a red sediment in acid urine that is soluble on heating always denotes uric acid, whereas a white sediment in alkaline urine that is insoluble on heating the urine alone, but readily soluble in warm urine after the addition of a little acid, denotes phosphates (*plus* carbonates and urates). Phosphatic sediments always appear when the urine is alkaline when voided, or becomes alkaline on standing (fermentation). The sediment may be crystalline or amorphous. The composition of the sediment can be determined by microscopical and chemical analysis. Only the most important sediments and the methods employed for their recognition can be discussed in this article.

URIC ACID (see Fig. 4861).—This sediment, as shown

in the drawing, may appear in a great variety of forms. Pure uric acid is white. The urinary uric acid is always colored red to dark brown from the admixture of urinary pigments. The crystals readily dissolve under the microscope on addition of potassium hydrate solution, and reappear in a short time as rhomboid crystals on addition of hydrochloric acid. Uric-acid crystals, as already stated, only occur in acid urine.

Urates.—Alkali urates appear as amorphous fine granules of yellow or reddish-brown color in acid urine, whereas ammonium urate occurs only in alkaline urine in the form of spheres that are surrounded by a wreath of fine needles or spiculæ. The morphologic characteristic of amorphous urates and of ammonium urate are represented in Fig. 4862. Urates are soluble under the microscope on addition of acids. On standing, crystals of uric acid appear.

Calcium Oxalate (see Fig. 4863).—These crystals present so typical a microscopical appearance that they be ruled out, the appearance of much calcium oxalate sediment should lead to the chemical estimation of the urinary oxalic acid as described above.

Calcium Sulphate (Fig. 4864).—This is a rare urinary sediment. The crystals are soluble in acids and in ammonia. The pathologic significance of these crystals is small.

Calcium Carbonate (see Fig. 4865) is a rare sediment of subordinate clinical importance. On addition of mineral acids the sediment rapidly dissolves. Under the microscope effervescence can be seen.

Phosphates (Figs. 4866 and 4867).—These salts appear in two forms, amorphous and crystalline. As already stated, alkaline urine always precipitates phosphates. If the urine is acid when voided, increased excretion of phosphates may be taking place and still no sediment form. As a rule, therefore, a phosphate sediment has only slight clinical importance. There is, however, a metabolic disorder that may lead to phosphaturia.

Fig. 4861.—Uric-Acid Sediment. (Original.)

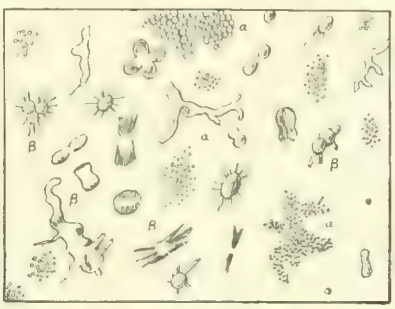


Fig. 4862. α, Amorphous urates; β, ammonium urate. (Original.)

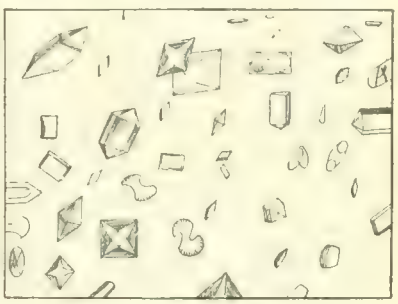


Fig. 4863. Calcium Oxalate. (Original.)

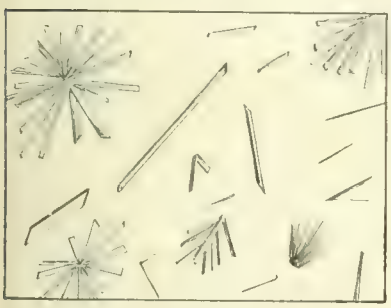


Fig. 4864.—Calcium Sulphate. (Original.)

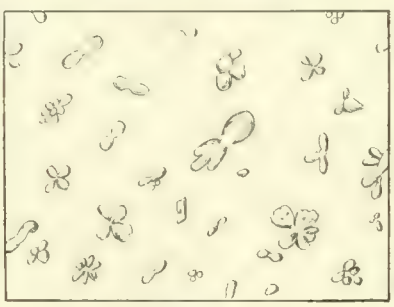


Fig. 4865.—Calcium Carbonate. (Original.)

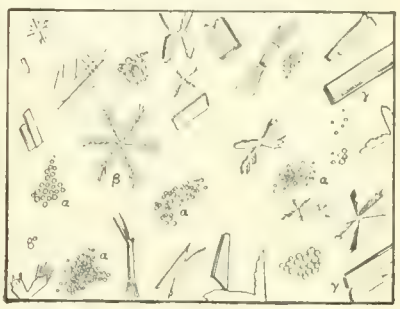


Fig. 4866. Phosphate Sediments. α, Amorphous earthy phosphates; β trimagnesium phosphate; γ, triple phosphate. (Original.)

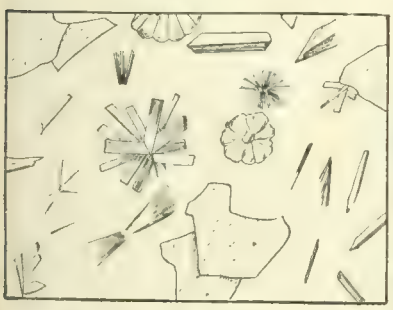


Fig. 4867.—"Neutral" or Dicalcium Phosphate. (Original.)

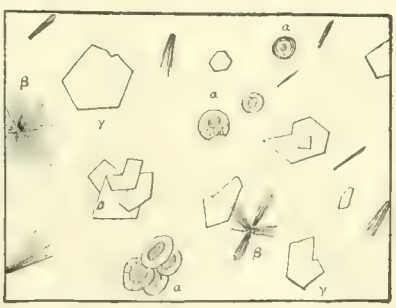


Fig. 4868.—Leucin, Tyrosin and Cystin. α, Leucin; β, tyrosin; γ, cystin. (Original.)

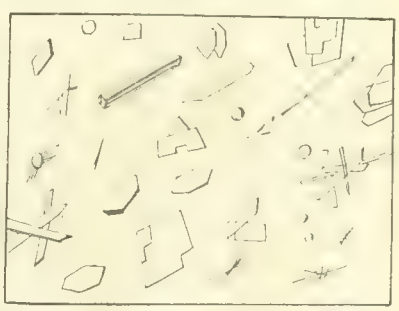


Fig. 4869. a, Hippuric acid; b, cholesterin; c, fatty crystals; d, urea nitrate; e, fat globules. (Original.)

cannot be confounded with anything else. They occur in normal urine, and may appear in large numbers after the ingestion of certain vegetables (asparagus, beans, carrots, etc.) that contain oxalic acid. If this factor can

We distinguish: (1) Amorphous earthy phosphates (calcium and magnesium phosphate); (2) trimagnesium phosphate; (3) dicalcium phosphate (stellar phosphate); (4) ammonium-magnesium phosphate (triple phosphate). (1)

Occurs in alkaline or neutral urine; (2) in concentrated alkaline urine; (3) in neutral or slightly acid urine containing large quantities of calcium phosphate. (4) chiefly in alkaline urine, particularly after ammoniacal fermentation. It may also occur in feebly acid urine. Needless to say that several of these phosphates may and often do occur together.

Leucin and Tyrosin (see Fig. 4868).—Leucin and tyrosin usually occur together. The microscopical appearance is characteristic. They appear in the urine in acute yellow liver atrophy, in phosphorus poisoning, and in a number of infectious diseases.

Chemically leucin crystals can be recognized by evaporating the crystals with HNO_3 on a piece of platinum foil. A colorless residue remains that forms an oily mass when touched with a solution of KOH.

Tyrosin treated in the same way with HNO_3 forms a yellow residue, that treated with NaOH gives a reddish color. If the mixture is evaporated to dryness a brown-black mass remains.

Or the crystals of tyrosin may be dissolved in hot water and the solution treated with KNO_2 and $HgNO_3$. The liquid turns dark red and precipitates a red sediment.

Cystin (see Fig. 4868, also section on "Cystinuria" above).—The appearance of cystin crystals calls for chemical analysis of the urine for cystin and quantitative estimation of the cystin excretion.

Other Unorganized Urinary Sediments may be mentioned for completeness' sake. They have no clinical significance whatever. The microscopic appearance of sediments of *hippuric acid, cholesterin, fatty crystals, urea nitrate,* occasionally forming on addition of HNO_3 to the urine, and *fat globules* (Fig. 4869), should be familiar to the clinician in order to avoid confusion with more important sediments.

Urinary sediments may also contain xanthin, blood pigment, bile pigment, indigo, and numerous accidental contaminations. *Alfred C. Croftan.*

URISOLVIN is a mixture of acid lithium citrate and urea, used in 0.2 gm. (gr. iij.) dose as a diuretic and uric-acid solvent. *W. A. Bastedo.*

UROPHERIN, theobromine-lithium salicylate, lithium-diuretin, $C_7H_7N_4O_2Li + C_6H_4OH.COOLi$, is prepared by mixing theobromine with the hydroxide and salicylate of lithium. It is a white powder soluble in five parts of water, and differs from diuretin only in the substitution of lithium for sodium. It is strongly diuretic in 1 gm. (gr. xv.) doses repeated frequently.

Uropherin benzoate is prepared from the benzoate of lithium instead of the salicylate. *W. A. Bastedo.*

UROSIN, lithium quinate, is made by mixing quinic acid, which tends to prevent the formation of uric acid, with lithium citrate, which is a uric-acid solvent. It is held by Weiss and by Sternfeld to be almost specific in attacks of gout. The dose is 0.5 gm. (gr. viij.), frequently repeated. *W. A. Bastedo.*

UROTROPIN, hexamethylene-tetramine, aminoform, cystamine, cystogen, formin, ammonio-formaldehyde, etc., $(CH_2)_6N_4$, is made by combining six molecules of formaldehyde with four of ammonia. It forms rhomboidal crystals of neutral or faintly alkaline reaction, and is soluble in 1.2 parts of water, slightly in alcohol, and scarcely at all in ether. In the urine it may be detected by the formation of an orange precipitate with a few drops of a saturated solution of bromine.

Introduced in 1895 by Bordet, this remedy has come into universal use as a urinary antiseptic. It is very rapidly absorbed, Casper finding it in the urine in ten minutes; usually the urine continued to give off formaldehyde for several days. In a few cases no formaldehyde was demonstrable though urotropin was constantly excreted, and Citron calls attention to the fact that formaldehyde is sometimes not liberated in strongly alkaline urine. The blood of a rabbit, to which Casper administered urotropin hypodermically, was shown to contain formaldehyde.

The drug has been recommended as a diuretic, a uric-acid solvent, and a urinary antiseptic and acidifier. Thompson considers its diuretic powers to be very slight, though other observers report considerable increase in the flow of urine following large doses. As a uric-acid solvent Casper found that neither a urotropin solution nor the urine of a patient taking urotropin had any effect *in vitro.* He discovered accidentally, however, that it caused complete cessation of all visible phosphate excretion in a case of phosphaturia.

It is in bacterial conditions of the urine, however, that urotropin finds its chief indication. In typhoid fever there is much evidence that the bacilli are prevented from developing in the urine; at Johns Hopkins Hospital the typhoid bacilli did not completely disappear from the urine, but were much diminished in numbers. Osler recommended the drug very highly in typhoid cystitis. In suppurative pyelitis and cystitis urotropin has the power of greatly lessening bacterial action, while at the same time it tends to diminish the alkalinity or increase the acidity. When the urine is strongly alkaline it sometimes fails to act. Cohn found no improvement in tuberculous cystitis or in cystitis following acute gonorrhœa, but Bangs and others advise its routine employment in gonorrhœa, as it tends to keep the urine antiseptic and to lessen the tendency of the gonococcus to invade the posterior urethra and bladder. A. R. Elliott, of Chicago, gives up to 6 gm. (℥ iss.) a day, though noting that the acidity of the urine may be so increased thereby as to cause irritation. But there are a number of reports of vesical irritation, hæmaturia, and even melæna following much smaller doses. W. Langdon Brown reports two cases of vesical hæmaturia from ten grains three times a day for eight days. Morton noted burning in the urethra and frequent micturition from twenty-four grains a day. Biss, in three hundred and eleven typhoid cases, noted irritation and slight hæmaturia twice. The general opinion seems to be that the blood comes from the bladder and not from the kidneys, though it is advised not to employ the drug in cases of nephritis. Eastman noted lowering of temperature and pulse. The ordinary dose of urotropin is 0.2–0.5 gm. (gr. iij.–viij.), and Nicolaier advises that 1.5 gm. (gr. xxiij.) a day should not be exceeded. It is best administered with plenty of water in small doses frequently repeated.

Loebisch has proposed the employment of urotropin as an intestinal disinfectant, its administration in intestinal putrefaction being more promptly followed by absence of indican in the urine than is the case with salol and other much-used drugs. It is absorbed very rapidly, however, and practically all of it is excreted in the urine; so it hardly seems probable that appreciable quantities of it can act in the intestine. Joseph Eastman thinks it may prove of value in puerperal sepsis. *W. A. Bastedo.*

URTICARIA.—Urticaria is an affection of the skin of which the salient characteristic is the occurrence of peculiar lesions called wheals. The description of wheals therefore covers in large part the objective symptoms of urticaria.

A wheal is a circumscribed elevation of the skin due to œdema of the corium. A typical wheal is the lesion produced in the average individual by the bite of a mosquito or flea. The typical wheal is slightly elevated, sharply circumscribed, with a flat or rounded surface, and of irregular or oval outline. The centre is usually pale and bloodless, but around this pale elevated centre there is an erythematous halo. The pressure of the edge of the finger nail on a wheal causes a slowly disappearing pitting, as in other œdema. The development of a wheal takes place suddenly. The first evidence of it is a rapidly appearing erythematous spot which itches, and upon which there suddenly develops a flat, œdematous swelling. The whole evolution of the lesion may occur in a few seconds. The duration is usually short, from a few minutes to an hour or two, though occasionally the le-

sions last for one or two days, and at times they persist for a week or more. Upon the disappearance of a wheal, if there has been no traumatism from scratching, no trace is usually left. At times, however, there is slight pigmentation, and if, as frequently happens, there has been vigorous scratching, inflamed papules or excoriations remain as a result of the traumatism.

As would be expected of so capricious a lesion there are numerous variations upon this typical wheal, and various subvarieties of urticaria are described according to the predominating form of wheals which characterize them. Wheals vary in size most widely. Typical wheals are usually from the size of a split pea to that of a finger nail. At times they are not larger than small papules and indeed are almost indistinguishable from ordinary inflammatory papules. They are frequently of the size of a twenty-five-cent piece, and in extreme cases are much larger. The writer has seen a wheal of which the elevation was not greater than a quarter of an inch, which extended around the chest from the median line in front to the median line at the back, and from the line of the nipple above to below the border of the ribs (*urticaria gigans*). Their shape is equally uncertain. Usually of more or less oval outline, they at times assume most irregular shapes, and, in persons whose skins are particularly susceptible to the production of wheals, they may be produced of any shape (*urticaria factitia*). In color they vary from inflammatory red to waxy white. If the œdema is intense enough to press out the blood from the capillaries, they show as a pale waxy centre with a narrow red periphery. Where the œdema is not so intense, or where the looseness of the tissues prevents extreme pressure from the œdema, the lesions are red in evidence of the hyperæmia. Occurring in tissues like the prepuce and eyelids, which are lax and offer, therefore, little resistance to the outpouring of serum, the lesions often form tumor-like œdematous swellings that closely resemble an inflammatory process in the same tissues (*urticaria tuberosa*). They are differentiated by their sudden appearance and equally sudden subsidence and the entire absence of pain. Very rarely the pressure of the extravasated fluid in the skin is sufficient to cause uplifting of the epidermis, so that the wheal is capped with a vesicle or bulla (*urticaria bullosa*). In still rarer instances the extravasation of serum is accompanied by enough red blood corpuscles to make the contents of these vesicles or bullæ hemorrhagic (*urticaria hæmorrhagica*).

In an acute attack of urticaria there is a sudden outbreak of wheals preceded and accompanied by more or less itching. There may be only a few lesions, or they may be innumerable. They occur on any part of the body, without symmetry and without any regularity of distribution. The acute attacks are often introduced by a transient systemic disturbance, with evidences of acute gastro-intestinal irritation. The temperature rises sharply three or four degrees, there are a rapid pulse, furred tongue, nausea and vomiting, and more or less prostration. At times evidences of a gastric crisis seem to indicate the involvement of the stomach in this peculiar angioneurotic process. The lesions themselves are characterized by intense itching. This itching may occur not only in the wheals themselves, but often at points where no wheals are present. The itching usually precedes for a few minutes the appearance of the wheals, and it persists during their continuance. It is somewhat paroxysmal in character, varying in intensity, without corresponding variation in the lesions. The itching varies in different cases and in different individuals, and according to the site of the lesions. Lesions in loose tissue may be accompanied by no itching whatever, while those occurring in dense thick skin and where the sensory nerve supply is richest, as on the hands and feet, are characterized by the most intense itching.

The course of an acute attack of urticaria usually extends over a few hours or at most a day or two, the disease passing away after the appearance of several crops of evanescent lesions. At times, however, the disease persists for weeks and months in successive outbreaks of the eruption, and in such cases is characterized as urticaria chronica, the term referring to the persistence of the process as a whole rather than to any peculiarity of the individual attacks. On the other hand, urticaria is persistent at times not only from the occurrence of repeated outbreaks of the eruption, but because the lesions lose their evanescent character and persist for days or weeks (*urticaria perstans*).

The *urticaria papulosa* of children, described by English dermatologists, is the best type of persistent urticaria. The characteristics of this form are the persistence of the lesions and the fact that the true urticarial wheals are followed by inflammatory papules which may persist for several weeks. It is readily seen that the occurrence of successive crops of wheals, which themselves persist for days or weeks and are followed by inflammatory papules which persist even longer, will produce an exaggerated picture of the urticarial skin. In such cases, as a result of scratching, we have inflamed papules, infected excoriations and more or less dermatitis, that results in thickening and induration of the skin. These cases in their most extreme type are strikingly similar to Hebra's prurigo. It is indeed not unlikely that they pass at times into true prurigo.

It is not an infrequent experience to see the vaso-motor mechanism so delicate that wheals may be produced at will by friction or other slight traumatism (urticaria factitia). In cases of acute urticaria this phenomenon is usual. In certain individuals this vaso-motor instability is inherent, so that factitious wheals may be produced at any time by slight traumatism, as drawing a line on the skin with a little force with a blunt stick or a finger nail. In such cases it is of course possible to produce wheals of any shape, so that names and elaborate designs may easily be written in wheals upon the skin (*dermographism*).

Urticaria tuberosa, urticaria bullosa, and urticaria hæmorrhagica have been referred to above. The peculiarities of the lesions of urticaria tuberosa depend almost solely upon their location at sites where the skin is very loose, and the lesions deserve no especial mention except to call attention to their somewhat confusing appearance at times. The lesions of urticaria bullosa and urticaria hæmorrhagica are usually seen in run-down individuals living under unfavorable conditions. Urticaria bullosa occurs most frequently in children. Urticaria hæmorrhagica is frequently associated with other evidences of hemorrhagic tendency, as hemorrhage from the mucous membranes, from the bowels and from the genito-urinary tract, and it is an evidence of a more profound systemic disturbance than usually exists in urticaria. Both of these forms of urticaria are rare.

The term giant urticaria is applied to urticaria which is characterized by the development of one or more wheals of very large size. They may be typical wheals, but most frequently they are rapidly developing œdematous swellings of pinkish color that bear a very striking objective similarity to an acute cellulitis. Such swellings at times present very slight if any resemblance to an urticarial wheal. They occur most frequently about the face and extremities, and often form tense, angry-looking swellings that for the time cause alarming distortion. Frequent sites of these lesions are the eyelid, the cheek, the nose, the lips, and the ear, and on such parts they may cause the most grotesque deformity. The larynx is not an uncommon site for their development, and their occurrence in that location may be the cause of distressing dyspnœa. Very rarely has it been found necessary to perform tracheotomy in such cases. Usually these large lesions occur singly, but they may occur in successive outbreaks or several large lesions may occur at one time. These lesions, like other urticarial wheals, develop rapidly, usually in the course of a few minutes, and after persisting for a shorter or longer time as rapidly subside. They are painless, usually unaccompanied by itching, and, unless they interfere with some important function through their size, are the source of little discomfort. There may be slight constitutional

disturbance such as occurs in other forms of acute urticaria, and typical urticarial wheals may accompany or alternate with these giant lesions.

Giant urticaria is frequently described as a separate disease under the title of Angioneurotic Œdema, or Acute Circumscribed Œdema. It presents, however, no essential difference from other forms of urticaria. Its etiology, its course, and the fact of its being frequently accompanied by ordinary urticarial lesions show its essential relationship to urticaria, and for that reason it is included here. All that is to be said about etiology, pathology, prognosis, and treatment of other forms of urticaria applies with unessential variations to giant urticaria or angioneurotic œdema. The original description of this condition is usually credited to Quincke (*Monatshefte f. prakt. Derm. u. Syph.*, 1882). The condition, however, had been accurately described, and its character recognized previously, by Bannister (*Chicago Medical Review*, June 20th, 1880).

Etiology.—Urticaria occurs at any time of life, but is most frequent in childhood. Among young children acute attacks of urticaria are very common, as a result of imprudent eating or slight disturbance of digestion.

In most urticarias two factors stand out prominently in the etiology. The first is individual predisposition; the second is the presence of some toxic substance which disturbs the local vaso-motor tone. There are other forms of urticaria besides those due to the disturbance of the vaso-motor mechanism of the skin by toxic substances, but they are relatively few.

Underlying the development of urticaria from all sorts of causes is individual predisposition. In certain individuals urticaria can be produced by the most trivial causes, such as the crawling of a caterpillar upon the skin, or the ingestion of the minutest quantity of some particular substance. In other individuals its occurrence is unknown. So violent an irritant as even the sting of a bee may not produce the smallest wheal.

The causes of urticaria may be divided into local and constitutional. Among the local causes of urticaria are especially to be mentioned the bites of parasites, such as fleas, mosquitoes, the various forms of pediculi, bedbugs, and the stings of wasps and bees. The lesions may also be caused by contact with stinging nettle, jelly fish, or caterpillars.

The constitutional causes of urticaria are numerous, but they are largely comprehended under various forms of intoxication. In certain individuals the ingestion of a particular article of food or of a particular medicine is followed by the development of an acute outbreak of urticaria. Among food-stuffs that may cause urticaria are: oysters, crabs, lobsters, and other shell fish; pork, sausage, and other similar highly seasoned meats; mushrooms, strawberries, tomatoes, cucumbers, and nuts. Among medicines: opium, chloral, the salicylates, copaiba, cubebs, quinine, turpentine, valerian, and various coal-tar products. The most frequently offending substances among the above perhaps are shell fish and strawberries, opium, quinine, copaiba, and cubebs. Another form of intoxication from without, which is now a very common cause of urticaria and is a connecting link between the causes of urticaria introduced from without and those developed within, is that from the antitoxins. Urticaria is the most frequent cutaneous manifestation following the use of diphtheria antitoxin. Somewhat similar are the urticarias which have been described from the absorption of hydatid fluid.

The forms of intoxication from within which may cause urticaria are numerous, but far and away the most important is auto-intoxication arising from the gastro-intestinal tract. Over-eating, constipation, and defective elimination are the group of factors most frequently seen in the causation of urticaria. Disturbances of the liver, particularly those which are accompanied by the presence of bile in the circulation, are at times responsible for outbreaks of urticaria. And the conditions which are vaguely described under lithæmia, gout, and rheumatism, of which the essential characteristic is a disturbance of the balance between assimilation and excretion or the presence of suboxidation products in the blood, are frequently responsible for chronic urticarias. Urticaria is also at times a result of malaria, and Matas has reported a case in which outbreaks of urticaria seemed to take the place of the usual malarial attacks. Anæmia is a factor which has to be frequently combated in the management of urticaria, and it occurs also at times in connection with albuminuria and glycosuria.

After auto-intoxication, in the etiology of urticaria, come the various factors which may be included under the head of the nervous causes of urticaria. The condition is seen with considerable frequency as a result of the nervous disturbances accompanying disorders of the genito-urinary tract, in pregnancy, at menstruation, and during lactation. It is excited at times by violent emotional disturbances, as grief, the dread of some impending crisis, or the shock of surgical operations. In particularly unstable individuals it may occur from such slight mental disturbances as anger, confusion, or surprise. Its occurrence as a result of rectal worms, phimosis, and similar forms of local irritation seems to indicate that at times it is due to reflex nervous irritation. The occurrence of urticaria in connection with nervous diseases is well recognized. This is rather frequent in functional nervous disturbances like hysteria. It is rarer in connection with organic diseases of the central nervous system.

Pathology.—Urticaria is distinctly an angioneurotic disturbance. There is a temporary disturbance of the vaso-motor control which results in a dilatation of the capillaries of the part and local hyperæmia. There is a rapid outpouring of serum into the tissues producing an intense œdema. This shows as a swelling of the skin which at first is pink, but as the pressure becomes greater the blood is driven out of the capillaries at the centre and there develops a pale bloodless area surrounded by a halo of hyperæmia. Microscopically the tissues show the evidences of intense serous effusion with more or less diapedesis of leucocytes.

Diagnosis.—The diagnosis of typical urticaria offers no difficulties. Indeed this is usually made without the physician's aid. The rarer varieties of urticaria, urticaria hæmorrhagica, urticaria bullosa, and angioneurotic œdema, may lead to some confusion. In the first two types there are usually evidences of typical urticaria sufficiently manifest to give the key to the diagnosis. In angioneurotic œdema or giant urticaria the suddenness of its onset, its rapid development, the freedom from pain, and the accompanying evidences of typical urticaria usually make the diagnosis from cellulitis, with which it is most likely to be confused, easy. The diagnosis of urticaria in itself, however, is the smallest part of the problem with which one has to deal in the cases. The far more difficult part is the determination of the causative factors. This, in cases of chronic urticaria, often taxes one to the utmost.

Prognosis.—In acute urticarias relief is easy. In chronic urticarias the success of treatment depends altogether upon the difficulty which attends the relief of the underlying condition, and the prognosis as to ready relief in such cases should be very guarded.

Treatment.—The curative treatment of urticaria is altogether a question of the elimination of the underlying trouble and the management of the various cases is along the line of rational therapeutics. In all cases the possibility of the disease being due to parasites should be borne in mind. Where any of these are found to be the cause, the treatment is of course that necessary for the destruction of the particular parasite.

The constitutional treatment of acute attacks of urticaria is simply a matter of the relief of the digestive disturbance which usually is the cause of it. If the cases are seen early an emetic may be indicated. More frequently, however, a brisk cathartic, such as magnesium sulphate, is all that is necessary. The after-treatment of these cases consists of keeping the bowels open, and keeping the patient upon a careful diet until the digestive dis-

turbance is relieved. Frequently an acute urticaria is the culmination of more or less continued digestive disturbance. In such cases the mercurial cathartics are particularly valuable.

In the chronic forms of urticaria permanent relief is usually the result of painstaking investigation into the causation. The questions of defective elimination, constipation, lithæmia, or some lack of balance between assimilation and excretion, particularly have to be taken into consideration. The first attention has to be paid to the digestion. The diet should be regulated, indigestible foods generally prohibited, and a bland, simple dietary followed for a time. The free use of fruits, contrary to the advice sometimes given, is in my opinion usually indicated, and the patient should drink plenty of water. Careful attention should be paid to elimination, especially by the bowels, and for this purpose the rather liberal use of aperients for a time is advisable. Of the aperients I think that calomel and blue mass easily head the list in value; after them come senna, podophyllin, sodium phosphate. In the gouty and lithæmic, alkalies and colchicum are useful. In stimulating elimination I have had excellent results from the daily hot bath, the patient staying in the bath for from ten to thirty minutes each day, so that free sweating occurs. In certain cases the nervous sedatives prove distinctly valuable; the bromides, acetanilid, phenacetin, and sulphonal are all at times useful. The various forms of opium are to be avoided, not only because of their adverse effect on elimination, but because of the marked tendency of opium itself to cause urticaria.

It cannot be emphasized too strongly that in all persistent cases of urticaria the question of elimination and the condition of the digestive tract deserve first consideration. After that the other factors, such as malaria, jaundice, anæmia, and other less frequent causes, are to be investigated, and when found present are to be treated along the usual lines. Rational treatment failing, certain remedies, used more or less empirically, have been found helpful. Quinine, the salicylates, belladonna, and strychnine are useful in certain cases. Calcium chloride has been recommended by Wright, and it has at times seemed to me to be of service. Among the remedies used empirically the one which has given me the greatest satisfaction has been pilocarpine. Given to the point of producing the slightest evidence of its physiological effects, it is valuable in relieving itching and giving the patients rest. In certain intractable cases without gastro-intestinal trouble arsenic is recommended.

Local Treatment.—The local treatment of urticaria is almost entirely directed to the relief of itching. For this purpose in acute attacks of urticaria one of the commonest and most useful measures is the alkaline or acid bath. A general bath or sponge bath with sodium bicarbonate usually immediately stops the itching. Equally good results are frequently obtained with similar baths of common salt. Either the salt or the soda bath is most effective when it is rather strong. In place of soda or salt, borax or ammonium chloride may be used with equally good effect. The strength, for ammonium chloride, is one or two ounces to the bath.

Similar baths with vinegar or other acids are often equally effective, but they are not quite so agreeable, and usually nothing is gained by substituting them for the salt or soda bath. In place of the bath alkaline or acid lotions may be substituted. As acid lotions, water and vinegar equal parts, water two parts and vinegar one part, or alcohol two parts and vinegar one part, may be used with good effect. A one- or two-per-cent. solution of carbolic acid with glycerin in water or in a boric-acid solution is a most excellent antipruritic in these cases. In place of the water the lotion is sometimes made more agreeable, and perhaps more effective, by the substitution of distilled extract of hamamelis. Other antipruritic lotions are made with liquor carbonis detergens, or camphor chloral, or resorcin in the strength of one to three per cent. in water. A lotion which I have found particularly useful in severe itching, where the skin is not broken, is camphor chloral and carbolic acid, each one to three per cent., in equal parts of distilled extract of witch hazel and alcohol. This may be made more cooling and more powerful by the addition of one to two per cent. of menthol. In certain cases the addition of an insoluble powder in suspension to these lotions is advantageous. For this purpose suitable powders are zinc oxide and calamine. These may be added to such lotions as have been suggested above in the strength of one or two ounces to the pint. A type of such a lotion, which has given me excellent service, is the well-known calamine and zinc-oxide lotion, with the addition of one or two per cent. carbolic acid and glycerin. A good formula for this lotion is as follows: Acid carbolic, glycerin, āā ʒ i.–ʒ iij.; zinc oxide, calamine, āā ℥ i.–℥ ij.; lime water, Oj. Frequently a most agreeable application, in conjunction with these other measures, is a dusting powder to be applied after the bath or after the application of a lotion. Suitable dusting powders for this purpose are zinc oxide, starch, talcum, or stearate of zinc. A useful addition to these powders is boric acid in the proportion of one-half to one drachm to the ounce, or salicylic acid, resorcin or thymol in the proportion of five to twenty grains to the ounce. Usually, unless there is a secondary dermatitis, ointments are not desirable. They are mussy and inconvenient and dirty and not more effective than the lotions. Where there is a secondary dermatitis, however, as a result of scratching, ointments are frequently useful not only as vehicles for the active medicament, but as a protection for the abraded surfaces. In such conditions the antipruritic lotions have to be used with some care, as they are more or less irritating. Baths are not contraindicated, but the addition of bran or oatmeal to the baths in sufficient quantities to make them slightly mucilaginous renders them more soothing. *William Allen Pusey.*

URTICARIA PIGMENTOSA.—Urticaria pigmentosa is a rare affection which is characterized by the development of wheals which are followed by peculiar persistent pigmented macules or nodules. It differs in many respects from ordinary urticaria, and, although the disease is accompanied by wheals, it is in all probability not a form of true urticaria. Two forms of the disease exist—the macular and the nodular. These at times occur distinctly, or more frequently the disease presents a combination of the two types. All forms begin in early childhood. The first evidence is the development of erythematous spots, which are followed in a day or two by the development of small reddish wheals. In other cases wheals develop suddenly without any noticeable premonitory erythema. In the macular form, upon the disappearance of the wheals there are left fawn-colored or brownish-yellow pigmented stains. These are level with the skin or perhaps slightly elevated. In the nodular form there is the same sudden eruption of wheals which are succeeded by nodular lesions that remain indefinitely. These are at first reddish, but in time become brownish-red or brownish-yellow. Similar lesions continue to appear and the disease thus goes on for many years. Individual nodules may persist for years; at other times they shrink and disappear, leaving brownish, pigmented, atrophic spots. Usually after several years new lesions no longer develop and the disease gradually disappears. In both the macular and the nodular forms factitious urticaria can be produced by friction, and in the same way wheals may be made to develop at the site of the nodular or macular lesions. Itching in these cases is usually severe, and, continuing as it does for years, is the most serious feature of the disease.

Etiology.—Its cause is practically unknown. It appears usually within the first six months of life, most frequently before the third month, and only a few cases developing after eighteen months have been recorded. Most of the recorded cases have been in boys.

Pathology.—A section from one of the lesions shows no alterations in the epithelial layer except marked increase of pigment in the basal layer and some horizontal stretch-

ing of the epithelial cells. The upper part of the corium is œdematous, and there is a peculiarly abundant infiltration with mast cells. Unna was the first to call attention to the marked accumulation of mast cells in the corium, and his observations have been repeatedly confirmed by other observers.

Diagnosis.—The extreme rarity of the disease renders it liable to be overlooked. The presence of factitious wheals and itching suggests urticaria, and when there is added to this the presence of the peculiar brownish-yellow persistent nodules or macules, the diagnosis should readily suggest itself. There is no other disease that closely resembles it. The diagnosis from urticaria is made by the presence of the peculiar persistent lesions. The process might also suggest xanthoma, but the lesions of xanthoma are of a distinctly yellow color, while these are dirty-yellow or brown. Xanthoma does not itch, and has none of the other features suggestive of urticaria.

Prognosis.—The disease usually persists for years, at least until the time of puberty, although some cases have been known to get well after a duration of one or two years.

Treatment.—Treatment has had no effect upon the course of the disease. Relief of digestive disturbances renders the disease less severe, and careful attention to the dietary of the patients has some effect in improving their condition. Crocker reports that the empirical use of Fowler's solution had a marked effect in preventing the development of new lesions in one of his cases. The itching can be in great part controlled by the use of antipruritic applications, such as are used in ordinary urticaria, and the local treatment is along the same lines as in urticaria. *William Allen Pusey.*

USTILAGO.—(*Corn-smut, Corn-ergot*, etc.) The fungus *Ustilago Maydis* Leveille, replacing the grain of *Zea Mays* L. This well-known blight of Indian corn grows upon various parts of the plant—stem, leaf, sheaths, tassels, but especially upon the forming ears. It forms early a fleshy, irregular mass of mycelium embedded in a jelly-like substance, and attains upon the ears, which it transforms or destroys, a size equalling that of a cocoanut, more or less irregularly globular. At maturity it develops into a black, dry, crumbly, or powdery mass of spherical, tuberculated spores enclosed in a cellular pouch. It has an unpleasant musty odor and taste. This ripe mass of spores is the portion used, and it is collected in midsummer, simply freed from impurities and dried. As obtained, it is a mass of powder and shreds of membrane, nearly as black and quite as dusty as powdered charcoal.

Little is known of the constituents of ustilago, except that they are, in a general way, similar to those of ergot. Mitchell has found that in frogs it soon acted as a narcotic, destroying consciousness; it then paralyzed the sensory centres in the spinal cord, and afterward, if the dose were toxic, the motor centres and nerves.

Numerous clinical reports have been made to the effect that it acts upon the parturient uterus much like ergot. Its use was considerably urged from 1876 to 1880, and it became official in the United States Pharmacopœia of the latter year, but its use has now almost altogether ceased. It has also been given in menorrhagia, bleeding fibroids, and other troubles which may be relieved by increasing the tension of uterine tissue. Dose, in infusion or fluid extract, from 1 to 3 or 4 gm. (gr. xv. to lx.).
W. P. Bolles.

UTAH HOT SPRINGS.—Box Elder County, Utah.
Post-Office.—Utah Hot Springs Hotel
Access.—Viâ Southern Pacific and Union Pacific Railroads. The Utah Hot Springs Company's Steam Motor Line runs in connection with the Ogden City Street Electric Line.

These springs flow from the western base of the Wahsatch Mountains into Salt Lake valley, about nine miles north of the city of Ogden. They are located at an elevation of 4,246 feet above the sea-level. The mountains here are very rugged and picturesque, and attain an elevation of more than 5,000 feet above the location of the springs. As shown by the reports of the United States Signal Service, the climate of the Salt Lake valley is very mild in winter and free from oppressive heat during the summer months. The atmosphere is very invigorating and beneficial to almost all classes of invalids. There are three large springs in the group, and when discovered they resembled three immense wells, twenty to thirty feet in diameter, and eighty to one hundred feet deep. Each of these furnishes a large stream of clear, hot, sparkling water, their combined outflow being about 160,000 gallons in twenty-four hours. The temperature varies from 131° to 144° F. An analysis by Prof. Spencer F. Baird, Smithsonian Institution, Washington, D. C., resulted as follows:

One United States gallon contains (solids): Calcium sulphate, gr. 18.07; calcium chloride, gr. 170.49; potassium chloride, gr. 97.74; sodium chloride, gr. 1,052.47; magnesium chloride, gr. 1.07; magnesium carbonate, gr. 11.77; silica, gr. 2.69; alumina, gr. 0.25. Total, 1,354.55 grains. Carbonic acid gas, 37.18 cubic inches.

The Hot Springs Hotel is a frame structure, about three hundred feet long, the north end of which is used for baths. The resort is very well supplied with bathing facilities, containing, besides many private rooms, a large plunge bath for women and another for men, and an immense swimming pool. The water is quite strongly muriated saline. It contains, in addition to the mineral ingredients, a large amount of organic matter in the form of vegetable growths or algæ. These form rapidly in reservoirs containing the water, and, it is said, they impart a soft, unctuous, or oleaginous effect to the water, which is very pleasing to the skin, and believed to be soothing to the nervous system. The baths are much resorted to by persons suffering from rheumatism, gout, syphilis, chronic bronchial catarrh, obstructive jaundice, disorders of menstruation, etc.
James K. Crook.

UTAH WARM SPRINGS.—Salt Lake County, Utah.
Post-Office.—Salt Lake City.

These springs are situated at the base of the heights of Ensign Peak, in West Second Street, Salt Lake City. The location is about 4,060 feet above the sea-level, or 20 feet above the general level of the Salt Lake valley and 40 feet above the lake itself. The springs are the property of the city, and are leased by the present managers for a period of ten years. An excellent bathhouse, easily accessible from all parts of the city by electric cars, is maintained at the springs. The water has a temperature of 112° F. as follows. It was analyzed by Dr. Charles T. Jackson, of Boston, with the following results: One United States gallon contains (solids): Calcium and magnesium carbonate, gr. 10.22; iron peroxide, gr. 1.70; calcium, gr. 23.21; chlorine, gr. 147.14; sodium, gr. 125.66; magnesium, gr. 15.86; sulphuric acid gr. 29.94. Total, 353.73 grains. *James K. Crook.*

UTERUS. See *Sexual Organs, Female*, and *Gestation*.

UTERUS, DISEASES OF: AFFECTIONS OF THE CERVIX.—In considering diseases of the cervix uteri, it must be remembered that the cervix is an integral part of the uterus, and that disease of one part is generally coincident with disease of the whole. The fact remains, however, that disease of the cervix does occur without invasion of the corpus uteri and *vice versa*.

Atrophies

1. Physiological Atrophies.—*Senile Atrophy.*—Generally with the commencement of the menopause a change in the size and consistence of the cervix takes place in conjunction with changes of a like character which occur at this time throughout the whole genital tract. Instead of at the usual time these changes may appear much earlier in life, and their premature onset, without pre-

vious sickness or known cause, is simply an early physiological ending of the active sexual life.

The cervix becomes reduced in size and assumes a conical shape, the mucous membrane loses its pink color and is pale and anæmic; while the folds of the arbor vitæ atrophy and in some cases almost disappear. The epithelial lining of the cavity undergoes retrograde changes, so that the secretion almost or wholly ceases and the canal may be hardly patent. Oftentimes the cervix nearly disappears, and owing to the atrophy of the vaginal fornices remains only as a dimple in the apex of the cone-shaped vagina.

With the cessation of menstruation we have the well-known general symptoms, be it early or late, but the process in the genitals being a physiological one requires no special treatment.

Under physiological atrophy may also be included the change which takes place after castration; the process and symptoms which follow being analogous to those of senile atrophy.

Atrophy of Lactation.—It has long been a well-recognized fact that the uterus of a woman nursing her child contracts more quickly and firmly, due to a reflex action upon the uterus. This may go so far that the uterus is smaller than normal.

While this process is perfectly physiological, according to those who have made careful observations on this subject, yet it may go so far as to become pathological in women upon whom the strain of nursing is too severe, or who are suffering from debility. Horn, who has investigated this subject very thoroughly, says that with the return of menstruation the uterus regains its former size. He also found that the atrophy was of two distinct kinds. In one class the uterus became pale, anæmic, and small, with the cavity diminished in size. In the other the walls became thin and flabby and the cavity diminished. The cervix was affected in some cases, while in others it took no part in either form of atrophy. When the atrophy is not of the severe type the cervix is little altered, but with the involvement of the whole genital tract it is markedly affected and becomes small and short.

Prognosis in the lactation atrophy, when the process has not been allowed to proceed too far, is good, even when there is some local or bodily ailment.

Treatment is not usually required, as with the return of menstruation and sexual intercourse the uterus regains its former size. In instances in which there seems to be danger of the atrophy proceeding too far, the child should be taken from the breast and the patient given rest and tonics. If more is needed, treatment should be directed to increasing the blood supply of the uterus by passing sounds, by the use of hot douches, by massage after Brandt's method, or by painting the cervix with Churchill's tincture of iodine. Hot sitz and foot baths, as well as scarification, may also be tried.

2. Pathological Atrophies.—*Atrophy Following Systemic Diseases.*—This has been reported following tuberculosis, diabetes mellitus and insipidus, myxœdema, nephritis, Addison's and Basedow's diseases. Cases have also been seen after scarlet fever and typhus fever, articular rheumatism, after paralysis of the lower limbs, from the morphine habit, and from psychical derangement.

Atrophy Following Infection of Uterine Adnexa.—The process here is decidedly different from that of the physiological atrophies. Instead of the simple reduction of the individual muscle fibres as regards size, necrosis and degeneration take place, and large pieces of the uterus may be thrown off, with contraction as an ultimate result. Thrombosis of the veins has been shown to take place with loss of muscular structure and mucosa. The connective-tissue formation and its subsequent contraction cause the reduction in size in the last named.

Infection of the ovaries and the destruction of their function lead to the same results as are seen after castration.

Prognosis in puerperal infections, as regards the ultimate recovery of the uterus from its atrophic state, is especially poor, as the tissue changes are far-reaching and usually beyond the hope of regeneration. The outlook is especially grave when there is great atrophy of both cervix and corpus, or when the inflammatory process has extended to the ovaries.

The acute infectious diseases cause as a rule a temporary atrophy, which soon disappears with the restoration of bodily health.

The prognosis of the uterine changes in the chronic systemic disorders is practically that of the associated disease, for in such instances it is only the local manifestation of a general process.

Treatment of all these cases is usually unsatisfactory, as the pathological changes place the tissues beyond a chance of repair.

Hypertrophies.

Hypertrophy of the Cervix.—Chronic metritis is the cause of this rather rare condition, which, as in chronic inflammatory processes elsewhere in the body, brings about a large increase in connective tissue. The muscular structure undergoes fatty degeneration, and bundles of fatty fibres are found enclosed by large bands of connective tissue. Sometimes the blood-vessels are varicose, and sometimes, cut off by these strong connective-tissue bands, their lumen is diminished and the circulation of the part impeded, bringing as a result chronic passive congestion. The entire uterus may be affected and show on section white shining bundles of tough connective tissue with the degenerated muscle fibres between, and small hemorrhages from the walls of the varicose vessels. Occasionally these changes are limited to either the cervix or the body of the uterus; but even when so limited, the remaining part is seldom or never entirely intact. In some instances the hypertrophy of the cervix makes the body appear like a small appendage, and the relations of the body and cervix are as in the child, in whom the cervix forms about two-thirds the entire uterus.

When there is a pre-existing injury of the cervix the lips often spread far apart, become greatly enlarged, and form a knob on the end of the much elongated cervical neck.

Enlargement of the cervix, due to obstruction and retention of the contents of the cervical glands, as the result of endocervicitis, is exceedingly common. It is most often seen after the lacerations and infections of childbirth. The mucous membrane is of a bluish appearance, or at times may appear quite bloodless. The small cysts may give no hint of their presence to the eye, but to the touch they are apparent in all sizes, studding the cervix like small shot or peas under the mucous membrane. They may attain the size of a small marble. At times they stand out like sago grains under the mucous membrane, which is usually hyperæmic, while the so-called erosions are apt to be present, stimulated by the irritating discharges from the cervix. On puncture a clear, cloudy, or even sometimes blood-tinged mucoid substance exudes and the mucous membrane of the gland is seen as the bright, glossy covering of the cyst wall.

As a rule this form of enlargement does not reach the extent of the true hypertrophy, and the cervix usually remains soft and bleeds easily; still it may lead to such contraction and cirrhosis that operations upon such a cervix are practically bloodless. Occasionally, through the increased size of the uterus and cervix, and the relaxed condition of the tissues of the pelvis which generally accompanies the increase in size, the cervix may appear at the vulva. The acid discharges from the cervical canal are irritating to the vagina and external genitals, and are probably the cause of sterility in such cases.

Hypertrophic Elongation of the Infravaginal Cervix.—This is generally a congenital affair, but the form which is considered here is the result of metritis, and so belongs properly to the hypertrophies. The process is the same as previously described. It is accompanied by the general symptoms common to most uterine displacements, and may be the means of furthering a procidentia, as the increased weight of the uterus drags it downward with the long cervix to guide it through the vagina.

Hypertrophic Elongation of the Supravaginal Cervix.—Elongation of the upper segment of the cervix is fairly common and is a mechanical process. The body of the uterus remains fixed in the pelvis either by adhesions or by the strength of its utero-sacral ligaments, the corpus being often retroverted. As this form seems to occur in women who are physically reduced and whose tissues are relaxed, or in cases of subinvolution of the tissues of the pelvis after pregnancy, it seems due to a loss of the normal resiliency of the tissues. The uterine neck is dragged upon by the vaginal wall and so stretched that the cervix may reach the vulva. The bladder wall is always said to descend first and then the posterior wall of the vagina. Coupled with this stretching there is always a certain amount of hypertrophy; but more frequently the neck of the uterus can be felt as a long thin cord stretching up to the body. It is evident that tensile elongation is present; for if the woman lies upon the back, the uterus returns to nearly its normal size, and will undergo still further reduction in size if the patient remains in bed for a few days. For this reason it is always best to examine patients complaining of this trouble in a standing position. There is always apt to be great swelling of the vaginal portion of the cervix with ectropon of the mucous membrane.

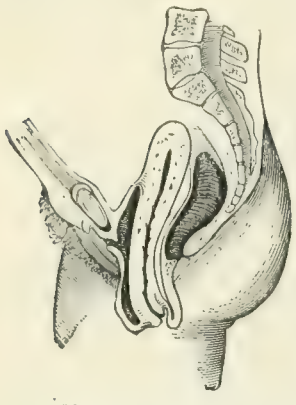


FIG. 4870. — Hypertrophy of Supravaginal Portion of Cervix, showing obliteration of vaginal fornices and descent of vaginal walls. (Schroeder.)

Occasionally cases are seen in which the uterine body feels like a small protuberance on the front of the elongated cervix as it lies in the cavity of the pelvis. This condition may also occur at the time of the climacteric.

Treatment of hypertrophy of the infravaginal cervix is usually rather unsatisfactory, as it is seen as a rule in the later stages when the harm has been done and its effacement is impossible. If the disease comes under observation early in its course considerable can be done, by first removing all the diseased mucous membrane with the sharp curette, and then using tampons of glycerite of tannin, or of ichthyol, or hot douches, with now and then an application of strong tincture of iodine to the cervix. Astringents may be used in the douches as well. By these means the venous congestion is relieved and absorption stimulated. At times puncture of the cervix seems to aid in the reduction in size, after the principle of the old-time leech, which now in the days of asepsis has almost disappeared. As the sufferers from these affections are generally in poor health, tonics suited to the general requirements of the case are indicated. Most important of all is proper hygiene, both as regards the body and as regards the sexual relations; the patient should be enabled to secure proper and sufficient food coupled with rest, freedom from care, and plenty of fresh air.

FIG. 4871.—Hypertrophy of Infravaginal Portion of Cervix, showing vaginal fornices in normal position and no descent of vaginal walls. (Schoeder.)

The bowels should be freely moved daily, and the use of calomel in small doses, extending over a period of some months, is said to have a very beneficial action in some cases. Ergotin has also been given in doses of from three to ten grains daily, but the patient must be watched for symptoms of ergotism where the remedy is continued for some time. Puncture with the galvano-cautery and the application of electricity have both been recommended; but the cautery only aids the process which is being combated, while the application of electricity is fraught with more or less danger, and the writers consider it of very doubtful efficacy. In some hypertrophies of moderate size a retroversion pessary may give relief when the conditions are favorable. By this means the feeling of weight is relieved and the tendency to procidentia prevented.

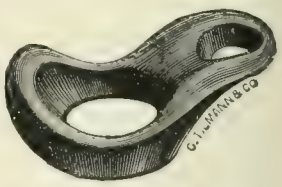


FIG. 4872.—Fowler's Pessary.

Whenever the more simple methods fail, the only aid lies in reducing the size of the cervix by some surgical operation. A wedge-shaped piece may be excised from each side, and the new anterior and posterior lips so formed should then be brought together as in bilateral lacerations of the cervix; or one of the various means of amputation may be tried. If a laceration of any extent already exists, the excision can be made during the repair of the cervix. This treatment always seems to have a very favorable effect upon the metritis which usually exists in the body, and of which the enlargement of the cervix is but a part.

The treatment of the hypertrophy of the cervix due to excessive glandular formation and retention cysts of the Nabothian follicles, must be primarily based upon the cure of the coexisting endocervicitis and endometritis. In the mild cases the small cysts may be punctured and the lining membrane destroyed with strong iodine, or carbolic acid, or nitrate of silver fused on the end of a probe. An elliptical piece may be snipped from the wall of the larger cysts, to prevent closure, and the inside curetted, or they may be treated in the same manner as the smaller cysts.

In the severer types of the disease many small cysts will be felt deeply embedded in the tissues. As a part of the treatment depletion and the hot astringent douches will be found useful.

For the milder grades of endocervicitis and endometritis applications of tincture of iodine and carbolic acid, or of forty-per-cent. formalin, may be tried; but it is the opinion of the writers that the danger is much less in the more severe cases if a curetting with aseptic technique is carried out. When the mucous membrane is extensively diseased, as is often the case in considerable lacerations, and if the lips are filled with cysts, the simplest and best method is to dissect away the diseased membrane as far as may be necessary, after the operation of Schroeder. If a bilateral tear exists it often is possible to remove the diseased tissue in the process of repairing the cervix. Should it seem best, a light packing of iodoform gauze may be placed against the cervix after Schroeder's operation, to prevent effusion between the raw surfaces.

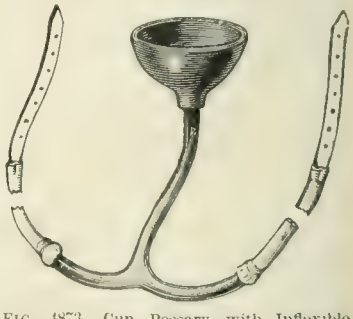


FIG. 4873.—Cup Pessary, with Inflexible Stem and Bands for Attachment to Waist Belt.

Hypertrophic elongation of the cervix when moderate

in degree requires treatment only by mechanical means. The indication here is to change the position of the cervix so that its axis does not correspond to that of the vagina. This can be done by means of a retroversion pessary having a bar across to hold the cervix in front, or by the well-known Fowler's pessary, which receives the cervix in a cup at its upper end (Fig. 4872). Of course this treatment is suitable only in cases in which the inflammation has subsided and the perineum is capable of supporting a pessary. The cup pessary can be tried when the vaginal method fails; but it has the great disadvantage that even with skilful and careful use it is apt to cause excoriation, and when the parts are not carefully watched, the pessary may give rise to the development of both recto-vaginal and vesico-vaginal fistulæ. This instrument is made like the cup of the old game of cup and ball. The cervix rests in the cup, while through the lower end of the stem pass the rubber tubes, which form the perineal bands and are attached to a waist band. This is at the best a clumsy appliance, and worthy of use only in cases in which for some reason the operative treatment is refused or contraindicated.

Amputation of the cervix constitutes the surest method of affording relief. This takes away the weight which drags down the uterus and at the same time removes the guide, which, if there is a tendency to procidentia, steers it through the vaginal canal. This may be all that is required; but if there is a ruptured or relaxed perineum it should be repaired at the same time. In case this does not suffice, ventral suspension to maintain the uterus in its proper axis still remains, or total extirpation.

Fig. 4874.—Hegar's Amputation of the Cervix Uteri.

Amputation of the cervix has been performed with the écraseur and also with the cautery; but the knife has taken the place of these methods which are prone to cause stenosis. To Hegar is due the credit of having invented the first really practical operation for amputation of the cervix—one which with slight variations is applicable to most cases. The cervix is split on both sides as far as to the vaginal junction, and a cone-shaped piece is then removed from each lip, according to the need of the individual case. The sutures are passed under the whole denuded surface from the cervical mucous membrane to that of the vagina. This may be continued all around, or, after suture of the central portions above and below, the sides may be brought together as in repair of the bilateral tears of the cervix. (See the section on Wounds of the Cervix, farther on.)

Schroeder's Method.—After lateral splitting of the cervix, as in Hegar's operation, the lips are held apart and the diseased tissue is removed, as shown in Figs. 4875 and 4876. The wound is closed by turning the flaps of vaginal membrane on to the denuded areas and stitching them in place. This brings the sutures into the entrance of the canal. The commissures on both sides are then brought together by sutures passing under the whole denuded area. There are some more complicated operations, but these two, with the modifications of which they are capable, will suffice in all cases.

The results of hypertrophic elongation of the supravaginal cervix are hard to combat by non-operative procedures. The relaxed condition of the vagina and its outlet, and the frequent presence of laceration of the perineum and of a retroverted adherent uterus, render the mechanical treatment of this condition exceedingly difficult.

In young women rest, astringent douches and tampons, and building up of the general health will usually bring

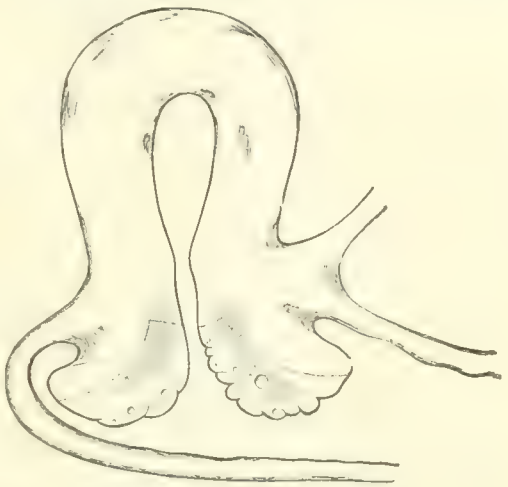


Fig. 4875.—Schroeder's Operation. Dotted lines show the extent to which the cervix should be denuded.

about a cure. As the uterus in these cases, which occur after childbirth, is generally retroverted, its support, after replacement, by some form of retroversion pessary is indicated.

The Hodge pessary may fulfil all the requirements if the lower end is made of such a width that it cannot escape from the grasp of the muscles of the outlet. If this is impossible on account of relaxed outlet, torn perineum, or adherent uterus, which resists well-applied packing in the knee-chest position, operation for repair of the pelvic floor and suspension of the uterus offer the

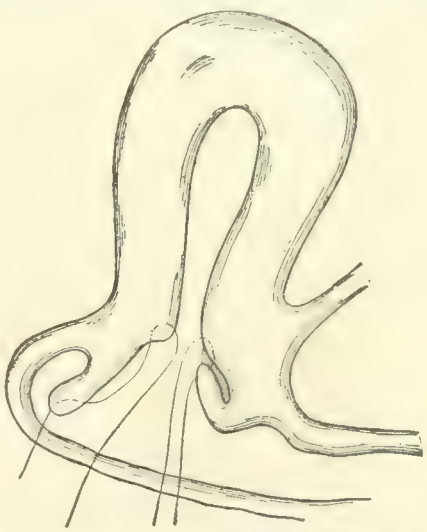


Fig. 4876. Schroeder's Operation. Diagram shows the manner in which the sutures are to be applied.

best chance of permanent relief. Pregnancy with the involution which follows it has been known to effect a cure.

At the time of the menopause or subsequently, the chance of effecting a cure except by some operative procedure is slight; but at the same time certain cases may be made comfortable for years. In the case of an ad-

lutent uterus it may be possible to hold up the prolapsing vaginal wall by the inflated rubber rings; but this, of course, is open to the objection that the walls are slowly stretched by their action, and that they are hard to keep clean. Gehrung's pessary (Fig. 4877) has been successfully used by some practitioners in retaining the vaginal wall in place; but a good pelvic floor is necessary for its retention. Generally speaking, the retroversion pessaries of all forms are not successful at this time of life, as the infravaginal cervix is atrophied and the vagina cone-shaped, while the perineum itself is too relaxed to retain them. As a last resort the cup pessary may be tried, but the many disadvantages, the care necessary to prevent excoriation and possibly worse consequences, may well make the gynecologist loath to use them in the majority of cases.

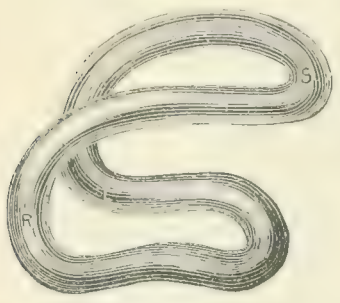


FIG. 4877.—Gehrung Pessary.

Should the discomfort and general condition of the patient warrant operation, the same principles will apply as when the disease occurs in early years. Furthermore, at the age when the sexual life is past, hysterectomy and a complete closure of the vagina by denuding its walls and uniting them with catgut throughout their length may be used as a last resort in obstinate cases. As we cannot expect the same involution of the tissues in older as in younger patients, operative interference is earlier indicated.

Ulceration of the Cervix.

True ulceration of the cervix occurs as the result of trauma or of systemic or local disease, and is very infrequent.

Chancroid of the cervix is occasionally seen and has the usual appearance of such lesions on mucous surfaces, except that, from the structure of the cervix, there is little œdema.

Owing to the moisture of the parts treatment is difficult. The cardinal points are cleanliness and dryness. If attention is carefully paid to these the lesion soon disappears, although to prevent further infection it is at times best to apply ninety-five-per-cent. carbolic acid or fuming nitric acid to the sore. The thermo- and the electrocautery have also been recommended. These applications should be carefully and sparingly made; this is especially true of nitric acid, which may produce bad sloughs and possible stenosis of the os externum. The vagina can be kept dry by a powder composed of equal parts of powdered starch and boric acid, or of compound stearate of zinc with boric acid or acetanilid.

Iodoform is strongly recommended by many, but its odor is very offensive, and it has no particular value over the odorless powders. The powders are best applied in the knee-chest position with the perineum retracted by a Sims speculum. The vagina is cleansed with pledgets of cotton dipped in borax water or a weak solution of bicarbonate of soda, by which means the mucus is easily removed. After cauterizing and drying the ulcer and vaginal walls, one or two teaspoonfuls of the powder are thrown on to and about the cervix, and the vagina is lightly packed with strips of gauze covered with the drying powder. These should be removed every twenty-four hours and fresh powder applied after wiping out any of the previous application which has become moist. The vagina is then to be packed as before. Indolent ulcerations may be touched with nitrate of silver, twenty to forty grains to the ounce of water.

Chancre of the cervix is comparatively rare, but more common than chancroidal ulcer. Rassenone found 117 cases among 1,375 cases of venereal sores of the genitals. Chancres occur more often on the anterior lip and may be multiple; occasionally they extend into the canal. They may be recognized by their well-defined border surrounding a depressed area covered by a grayish membrane. Beginning as mere erosions, they soon become deep ulcers, and instances have been reported of perforation into the rectum or into the bladder. They have been mistaken for cancer, and have been known to undergo cancerous degeneration after healing. Mucous patches are also seen among the secondary symptoms.

Constitutional treatment in a doubtful case will soon settle the diagnosis. As to local measures, douches of corrosive sublimate, 1 in 3,000 to 1 in 5,000, or treatment after the manner of the chancroidal ulcers with a powder of calomel and starch, will be found useful. Cauterizing is useless and may do much harm.

Tuberculous ulceration is very rarely seen, and is usually associated with the disease elsewhere, but may be primary. It may take the form of a simple ulceration or of lupus hypertrophicus, and is easily mistaken for cancer—a point which the microscope alone can decide in many cases.

The best treatment is probably the removal of the uterus and appendages, as they are generally infected. If this seems unnecessary, the cautery or amputation of the cervix may be tried. When the disease is too far advanced for operation the parts must be kept clean with douches of potassium permanganate or chlorinated soda in strengths suited to the comfort of the particular patient.

Atresia of the Cervical Canal (Acquired).

This is generally the result of lacerations due to delivery or to the action of caustics. It may result from contraction after amputation of the cervix, or after an operation for repair. Occasionally it results from the contraction of an old ulcer, from new growths within the uterus, or from old age. After the menopause this has no detrimental effect, unless, as occasionally happens, some infection takes place and pus is retained in the old uterine cavity. Previous to the menopause hæmatometra may be expected. Under such circumstances, if the atresia is at the internal os, the shape of the cervix is well preserved; but if it is at the external os, the cervix is carried up to a higher level and the entrance appears as a dimple in the vaginal vault.

Stenosis of the Cervical Canal (Acquired).

The causes are the same as for the preceding, and it occurs more often at the external than at the internal os. The cavity of the cervix may be contracted throughout its length, or, when the restriction at the external os keeps back the secretion, the cavity may be rather fusiform in shape.

Diagnosis of the condition may be made by inspection or by passing a sound or probe. As the tip of a small probe is often caught in the folds of the arbor vitæ, care must be exercised in introducing the instrument. Dragging down the cervix with the double hooks or tenaculum will sometimes obviate this difficulty by straightening the canal. Usually there is a slight spasm of the internal os, which gives way after a few moments of steady pressure. This must not be mistaken for stenosis.

Dysmenorrhœa is usually present and there is also sterility, but the first does not follow in every case, as women with a tight internal os often complain of no pain with the menses.

Pain is probably due to the fact that more blood is poured out from the uterine mucous membrane than can be taken care of by the narrowed canal of the cervix, while the distention of the uterus causes painful contractions of a paroxysmal nature. These are often relieved by the passage of a clot or a quantity of mucus. The pains may be so severe that vomiting, fainting, and various nervous manifestations take place.

The sterility is said to be due to the failure of the cervix to expel the mucus from its canal during the orgasm. It is probably also due to the endocervicitis which is present in these cases, and to an altered cervical secretion.

Treatment of stenosis is surgical, and what is said concerning this applies to atresia coming on before the menopause.

Electricity has been tried in the past, and while it may relieve for the time, the ultimate effect, as in the case of the caustics of the earlier days, is to leave the cervix in a worse state than that for which the treatment was undertaken. To-day four methods are in common vogue: gradual dilatation, discission, divulsion, and plastic operations,—all of which are necessarily contraindicated in any acute inflammatory disturbance of the uterus or adnexa.

Gradual dilatation is performed with Hanks' dilators, with the patient on the back or in Sims' position. The vagina is cleansed with soap and water, and wiped out with a solution of corrosive sublimate, lysol, or carbolic acid. The anterior lip is seized with the tenaculum and pulled gently downward. After the direction of the canal has been ascertained by means of a sound, the dilators are inserted in increasing sizes, each one being allowed to remain a few moments in the canal. For a lubricant lubrichondrin or glycerin may be used. The dilatation should not be carried so far as to cause fissures of the os, and one treatment a week is sufficient. Finally the canal is swabbed out with ninety-five-per-cent. carbolic acid or with tincture of iodine, and a tampon of ichthyol and glycerin is inserted. The latter should be removed the next day. Patients had best remain quiet for a time after the operation, as uterine cramps sometimes come on. No permanent results can be expected of this treatment, and it is advocated as a measure to be adopted only when pregnancy is desired. Probably the favorable results which follow are often quite as much due to the cure of the uterine catarrh as to the increase in the calibre of the canal.

Discission of the cervix with the various metrotomes, once practised so widely, has disappeared owing to the hemorrhage, sepsis, and contraction which followed too often in its wake.

Discission as practised to-day consists of splitting the cervix on each side as high as the junction of the vaginal wall and nicking the internal os on each side. The hemorrhage may be quite free, but is easily controlled by packing gauze between the lips. This operation is resorted to principally for the relief of stenosis and atresia of the internal os.

Divulsion or rapid dilatation under ether or chloroform narcosis and with aseptic precautions is almost devoid of danger, and is perhaps the most generally applicable method when the canal is patent. This is performed with any of the well-known cervical dilators, of which Goodell's modification of Ellinger's dilator is perhaps the best (Fig. 4878). The external genitals and vagina having been rendered surgically clean, the cervix is seized with the vulsellum forceps; and if the canal does not admit the tip of the special form of dilator used, it may be expanded with the Hanks dilators to the necessary extent. The blades of the dilator are then inserted under steady, gentle traction upon the cervix with the vulsellum forceps, and spread in all directions until the canal is dilated to from one-half to three-quarters of an inch. This may be followed by curettage, if necessary, and the uterus and cervix packed with iodoform gauze for from twenty-four to forty-eight hours. Curettage is necessary in most instances, as the stenosis may be due to the existing inflammatory condition of the mucous membrane, which is so common in these cases. Some operators prefer to insert a glass plug after operation in place of the packing, but with this there is increased danger of sepsis. Another advantage of the gauze is that it usually brings with it on removal any small pieces of the mucous membrane which have been skipped by the curette. It is also well to wipe out the uterine cavity before putting in the final packing.

The patient should remain in bed for ten days, and after the first two or three days the use of an antiseptic douche of creolin or lysol, 1 in 100, adds much to her comfort and cleanliness.

Plastic operations are used to relieve contraction or atresia of the external os when the cervical canal is dilated above. The principle of the many operations devised, which accomplish their purpose in the end results, is that involved in amputation of the cervix; and each case must be treated upon these principles, according to its needs.

Traumatic Affections of the Cervix Uteri

The position of the cervix deep in the pelvis affords little chance of injury except as the result of parturition, ill-fitting and neglected pessaries, inflammatory disease or the contraction caused by the indiscriminate use of caustics in the early days.

Abrasions.—Women wearing a pessary for the first time are liable to slight abrasions of the mucous membrane, even with the best of care. These are of no especial importance if taken in time; but, as often happens, the patient, feeling relieved, fails to appear for months, and the pessary becoming encrusted with salts causes not only excoriations, but ulcerations which may extend into the rectum or into the bladder. The external and internal combined pessaries are prone to cause these ill results, as they are generally bought of some instrument maker, often without any measurements being made, and are adjusted by the patient.

Also the support of the pessary from the outside by the elastic bands does not allow it to move freely with the excursions of the pelvic diaphragm without increasing the pressure. With the cup pessary, unless in the proper axis, the lips press against the cervix and cause sloughs.

The removal of the pessary and simple cleanliness suffice for the cure of the small abrasions. When the surface involved includes the vaginal wall as well, it is best after cleansing the vagina to apply some antiseptic powder and lay gauze between the abraded surfaces to prevent their adhering. Indolent or granulating ulcers may need stimulating or astringent applications.

Wounds of the Cervix.—Practically all lacerations of the cervix arise as the direct or indirect result of parturition, and are equally unavoidable. Broadly speaking, at least one-third of all labor cases have lacerations worthy of repair. Tears may occur from miscarriages in the early months, while delivery at full term may leave not the slightest trace of rupture. Portions of the anterior lip may slough from pressure, and large defects are sometimes caused in this way. Pregnancy occurring late in life for the first time, or after inflammatory disease, is apt, on account of the more resistant cervix, to leave its marks. Cases have been reported in which the resistance of the cervix to dilatation has been so great that it has been torn from the uterus by the force of the advancing head. The most severe injuries commonly result from precipitate labors, from manual dilatation, version, and forceps operations. These happen to the skilful as well as to the unskilful, so that it is not just to lay them at the door of the accoucheur, although of the neglect to repair them when necessary, he must bear the blame.

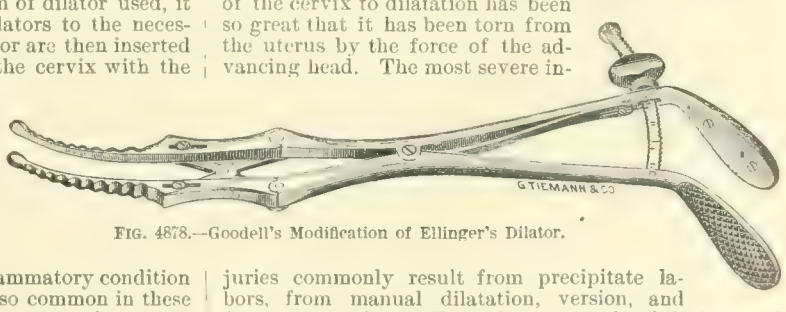


FIG. 4878.—Goodell's Modification of Ellinger's Dilator.

Finally, lacerations may occur from the tearing out of tenacula, double hooks, etc.

The fact that childbirth leaves its mark upon the cervix in so many cases makes it one of the surest guides as to the existence of previous pregnancy; but the fact must not be lost sight of that operative procedures may sometimes leave marks which simulate those of parturition.

Pathology.—Lacerations may be partial or complete.

A partial laceration is a tear of the mucous membrane and muscular substance which does not extend to the vaginal surface except at the external os.

A complete laceration is a tear through the whole substance of the cervix, laying open the canal for a greater or less extent; sometimes so far as the internal os.

These injuries in turn are designated by the terms unilateral, bilateral, stellate, according to the nature of the injury.

Unilateral lacerations are seen in all parts of the cervix, but are said to be more frequent in the left and posterior portions.

Bilateral laceration is the most common form, where the cervix is divided to a greater or less degree into an anterior and a posterior lip. After forceps delivery this is especially common from the pressure of the forceps exerted at these points.

Stellate lacerations, even when not deep, may cause gaping of the external os, and open the mucous membrane to the influences which cause the unpleasant symptoms of cervical laceration. Following manual dilatation multiple tears are quite common, and the ruptures may be so numerous that after labor the cervix has the feeling of a tassel.

As being the most frequent, bilateral laceration and its treatment will be considered, as what is said concerning it will be equally applicable to the other forms.

Following in the train of these injuries come certain pathological changes as a rule, the end results of which have a far-reaching effect upon the health of the patient unless the operation for repair is undertaken in time. Healing of the cervix after labor may take place; but for the most part the tendency of the lips to separate in the bilateral form keeps the torn surfaces apart, while the process of repair here, as in the other forms, is hindered by the constant flow of lochia over their surfaces.

The danger of infection of the parametrium is considerable when the tear reaches into the vaginal vault. The rolling out of the damaged mucous membrane from the gaping lips favors a state of constant irritation, and the opening up of the connective tissue of the pelvis presents the opportunity for infection. As a result of these conditions there is a constant hyperæmia, which ends in the formation of fibrous tissue and eventually renders the affected parts as hard as cartilage. Exactly as in cervical catarrh the inflammation may proceed so far that the cylindrical epithelium of the cervical mucosa oversteps its boundaries and extends on to the mucous membrane of the vaginal surface of the cervix, displacing the squamous epithelium. This is the "erosion of the cervix."

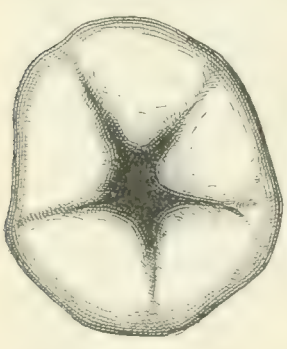


Fig. 4879.—Stellate Lacerations.

With the glandular hyperplasia comes increased secretion, while gradual occlusion of the glands by the new-forming connective tissue causes the Nabothian cysts.

The masses of cicatricial tissue so often felt about the uterus owe their origin primarily to these tears of the vaginal vault, and secondarily to the changes which take place in them as a result of infection; and in consequence of the contraction which subsequently takes place in these areas of new-formed tissue, displacements of the uterus in different directions are sure to follow. Subinvolution is very frequently seen after extensive injuries to the cervix.

In addition to the pathological changes which are found in the pelvis itself, various disturbances may take place, due not to the lacerations themselves, but to the irritation of the chronic metritis and endometritis with which they are so often combined. Furthermore, the increased weight of the subinvoluted uterus, when coupled with relaxed ligaments and a torn perineum, causes the organ to sag downward and adds to the effect of the diseased organs upon the system, the discomforts which arise from the loss of mechanical support. The unhealthy state of the mucous membrane is the cause of frequent abortions, and there is no doubt that cancer of the cervix is more common in cases which have suffered for years from these chronic inflammatory processes, of which the untreated injuries caused by childbirth were but the beginnings.

Symptoms.—The symptoms of fresh laceration of the cervix would be bleeding after the birth of the child, which could not be accounted for by a relaxed condition of the uterus or by a vaginal tear. Slight tears are always present, and it is only seldom that it is necessary to search for the point of hemorrhage at the time of labor.

Symptoms of cervix lacerations, as they are seen at more or less remote periods from the time of their occurrence, are quite variable. Sometimes there is pain on coitus, or, if a displacement is present in addition, the symptoms may refer more to the altered position of the uterus than to the injury itself. The extent of the injury is also no guide as to the seriousness of the symptoms. At times there is bleeding without apparent cause, and the menstrual periods are apt to be painful and accompanied by excessive flow. Leucorrhœa, often blood-tinged, is almost constant, and there is a feeling of general malaise. Reflex symptoms, neuroses of the stomach, eyes, bowels, and even hysteria may be present, while pain over the sacrum or in the lower abdomen is a frequent complaint.

Diagnosis.—The sense of touch enables one to form the best opinion as to the extent of a cervical laceration; for the introduction of a speculum, except in the knee-chest position, is apt to roll apart the lips and so obscure the exact condition. This is especially true in the bilateral tears. However, by seizing the upper and lower lips with tenacula and pulling them together, a good idea of the extent of the damage may be obtained.

When cysts are present in great numbers the feeling may be that of cancer, but inspection generally reveals the true state: the presence of small bead-like cysts, and of an inflamed, bulging mucous membrane, sometimes showing the plicæ palmatæ. Occasionally the condition presented may simulate hypertrophy, but by the drawing together of the lips the true state of affairs at once becomes apparent.

Palliative Treatment.—In the past, immediate repair of the cervix after labor has been recommended by some writers; but the consensus of opinion to-day is that operative procedure is not best until after the puerperium. The reasons for this are plain. After labor the cervix is bruised and some portions may slough. Also the tissue is so stretched and œdematous that correct coaptation of the parts is next to impossible, and with the rearrangement of the muscle fibres and subsequent contraction the sutures would become too tight and cut out. It is surprising to see how what appear like considerable lacerations at the time of delivery almost disappear when involution has taken place. Occasionally it may be necessary to insert a suture to control bleeding from the circular artery, but, as a general thing, a firm packing of the uterus and vagina, or even of the vagina alone, will cause the hemorrhage promptly to cease.

The larger number of patients with lacerations present themselves for treatment months or years after the injury has occurred. For this oftentimes the patients themselves are at fault more than their physician, as they defer the

examination after the labor and wait until discomfort, pain, or repeated miscarriages force them to seek relief.

Not every case of cervical tear demands operation. For the severe lacerations and their unpleasant symptoms operation offers the only lasting cure. For the slighter injuries, the writers believe that the degree of the existing endometritis and the density of cicatrix must be the guides.

When operation is contraindicated or refused, it may be possible to relieve the discomforts to a certain degree. The subinvolution and endometritis may be relieved by hot douches and by depletion with glyceride of tannin, ichthyol, and glycerin and boroglyceride. The patients should be carefully instructed in using the douche, both as to quantity and as to temperature. It should be taken while the patient is lying on her back, with the hips elevated, and at least twice daily. Not less than eight quarts of water should be used at a temperature as hot as can be borne. To this may be added disinfectants, or astringents, as alum or tannin. The reservoir should be just high enough above the patient for the water to flow very slowly, and at the end the reclining position should be maintained for from twenty to thirty minutes.

Cysts if present should be punctured and the exuberant mucous membrane painted with tincture of iodine, carbolic acid, or silver nitrate as often as may be demanded.

Fig. 4880. Denuding the Cervix.

Considerable relief is often obtained by these measures, and they often prove a valuable preparatory treatment for many operative cases.

Unfortunately the price of this relief is constant treatment, and with its cessation the old symptoms soon return.

Operative Treatment. — In considering the subject of operative treatment, the first question is to decide in what cases to advise operation. Every deep laceration is not in need of repair, and many comparatively slight ones demand more than palliative treatment. Generally speaking, it is the condition of the cervix and uterine body more than the extent of the tear which decides the treatment; but, as has been said, the more extensive the laceration, the greater likelihood of endometritis, ectropion, and the widely known "erosion." Instances are seen of widely gaping lips, which are soft and without the slightest sign of inflammatory disturbance. Such as these do not need operative interference. For the small laceration with much uterine catarrh and enlarged tender cervix, showing the effect of the irritating discharges, curetting of the uterus and depletion may prove sufficient. If the cervix is much hypertrophied and studded with cysts, curetting, the excision of a wedge from each side and uniting by the method of Emmet, or Schroeder's operation is to be advised. (See Amputation of Cervix, in the section on Hypertrophies.) Where very extensive disease is present, amputation is the best procedure.

As the climacteric approaches, repair is more necessary than in younger women, for it is well known that the lacerated cervix seems to be the starting-point for malignant disease.

Operation.—Emmet was the first to put the operation for the repair of the cervix before the medical profession, and his operation, with a few modifications, has stood the test of time and is applicable to most cases, although in atypical lacerations modifications must be introduced to suit the requirements.

The operation is performed either in the Sims' or in the lithotomy position. The bowels should be thoroughly

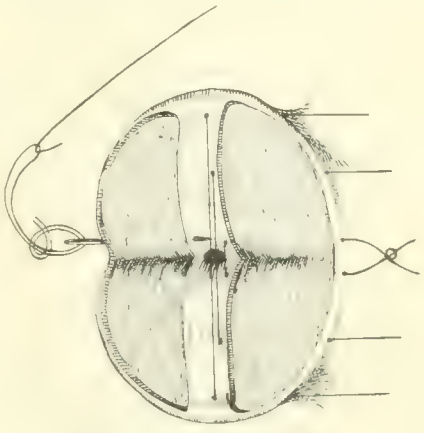


Fig. 4881. Sutures in Position.

moved the day before, and on the morning of the operation an enema should be given at least two hours before the time set for operation. The patient is given a hot douche of borax water, which clears away the mucus, and the hair on the genitals is clipped close. Under ether the external genitals are scrubbed with green soap and gauze, and douched with sublimate solution, 1 in 3,000. In case of very foul uterine discharges, it may seem best to curette the uterus and wait for a few days before operating upon the cervix.

The vagina is held open with specula, the cervix is seized with the double hooks, and the direction of the canal and the extent of laceration are determined with the sound. The cavity of the uterus is then curetted as a preliminary step.

With the tenaculum the posterior lip is seized in the centre and denuded, as shown in Fig. 4880. All the diseased mucous membrane and the cicatricial tissue which always forms in the apex of the tear, must be removed, only the mucous membrane in the line of the cervical canal—a strip from one-fourth to three-eighths of an inch wide—being left. The anterior lip is treated in the same way. If the hemorrhage is considerable, it can be readily stopped by packing a sponge against the cervix for a few moments.

For the denudation the scalpel is best, as it causes less trauma. Scissors can be used and the hawk-billed scissors of Skene are often useful in clearing away scar tissue at the apex of the wedge.

Suture material of chromicized catgut, silkworm gut, or silver wire may be used. Chromicized catgut has the advantage that it is unnecessary to remove the sutures. This is especially advantageous where an operation for lacerated perineum is to be performed at the same time.

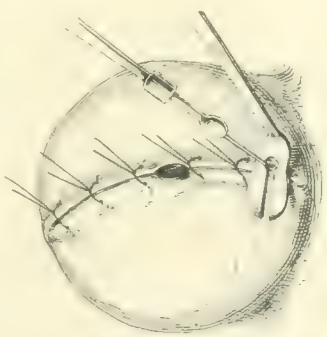


Fig. 4882.—Lips Approximated and Sutures Tied.

The manner of suture is also best illustrated by the figure. The first suture should be well up in the apex,

and each should pass from the vaginal surface under the whole denuded area and through the edge of the mucosa which has been left to form the new canal. Usually from three to five sutures on each side are sufficient. Sometimes, on account of the large amount of scar which has to be removed, it will be found necessary to cut away one strip of the mucous membrane which was left to form the new canal. This can be done without fear of atresia. It is generally better in operations upon the cervix not to pack the uterine cavity, as the removal of the gauze may tear out the sutures. Stellate and atypical lacerations must be repaired in a manner suited to each case. Where small tabs exist, they are often advantageously removed, especially if the cervix is enlarged, and the two adjoining edges denuded and sutured.

George Hareu.
Ernest Bogen Young

UTERUS, DISEASES OF: CONGENITAL MALFORMATIONS. — Development. — The uterus is formed by the approximation and fusion of the middle portions of the Müllerian ducts. The upper portions remain distinct, constituting the Fallopian tubes, while the lower unite and form the vagina. A vertical partition separates at first those parts of the ducts of Müller which go to make up the uterus and vagina, but this subsequently disappears, and the two canals become one. At a later period in the course of development, at the lower end of the middle third of the tube thus formed, the cervix appears, dividing the genital canal into uterus and vagina. The tissues at the summit of the middle third and between the points of origin of the Fallopian tubes likewise thicken, and the fundus uteri comes into existence. The insertion of the round ligament separates the upper from the middle third.

It is interesting to note that in the lower animals development regularly stops short at various points in the scale of progression, which ultimately ends in the formation of that which in the human female is a perfected genital canal, so that what in the latter are termed abnormalities, in the lower animals are the normal characteristics. At birth the cervix is longer and thicker than the uterine body, and this state of affairs persists throughout childhood. At puberty rapid growth occurs, and this condition is reversed, the cervix then appearing as an appendage to the body. By the twentieth year the genitalia have reached their full measure of development.

General Etiology.—Congenital malformations of the uterus are owing to a non-appearance of the elements

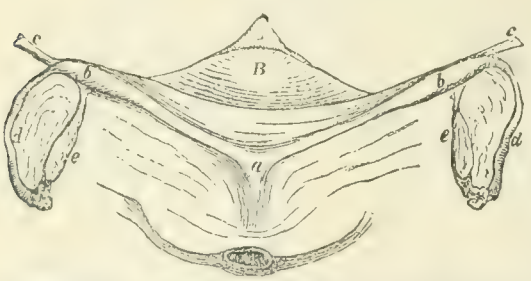


Fig. 4883.—Rudimentary Uterus, Posterior View. (After Veit.) *a*, Fused but solid portion of the uterus; *b*, *b*, uterine horns; *c*, *c*, round ligaments; *d*, *d*, tubes; *e*, *e*, ovaries; *B*, bladder.

which go to make up this body, to an arrest in their development, or to their complete destruction by nutritive disturbances, pressure changes, etc.

Classification and Nomenclature of Varieties.—The whole subject of congenital malformations of the sexual passages has been thrown into much confusion by the varying methods of arrangement and classification adopted by different authors, and still more so by the complicated and pedantic terminology that has been employed. The same name has been given to different conditions, and the same condition has received different

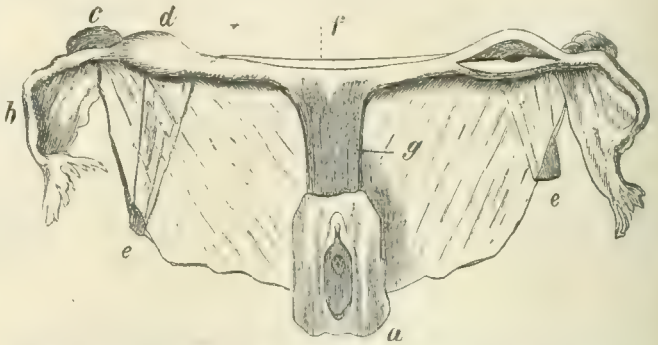


Fig. 4884.—Uterus Rudimentarius Bipartitus or Bicornis. (After Rokitansky.) *a*, Vagina; *b*, tubes; *c*, ovaries; *d*, enlargement of the horn; *e*, round ligaments; *f*, point of union of the two horns; *g*, cellular tissue traversed by muscle fibres which simulate the uterus in form.

designations. The classification and nomenclature which follows is that of Müller; it is at once the simplest and the most comprehensive.

I. Complete Absence of the Uterus: Defectus Uteri.—*Anatomy.*—Complete absence of the uterus, a condition rarely met with in viable subjects, is by no means uncommon in monstrosities incapable of life. Whenever encountered, other evidences of a serious blow to the progress of development are almost always present in some portion of the genital apparatus. The individual, in voice, habit, and general conformation adheres to the female type, but the organs which characterize the woman may, alone or in combination, be entirely wanting, or else may exhibit all grades of rudimentary development. Thus, with absence of the uterus it may be impossible to discover any trace of ovaries, tubes, vagina, or mammary glands; yet these structures may be present, though in a sufficiently undeveloped condition to render the proper performance of the functions severally peculiar to them a matter of doubt or of impracticability. Still, though this is true only of those in whom life is possible, the remaining organs characteristic of the female may be nearly perfect in their construction, and some, though rarely all, may correspond entirely with the normal type. The external genitals have been observed to be either normal or poorly developed, and in adults occasional absence of the pubic hair has been noted.

Etiology.—Defectus uteri is dependent either upon an entire absence or upon a complete destruction of the median portions of Müller's ducts.

Diagnosis.—The recognition of the abnormality under discussion is surrounded with the utmost difficulty, and it is never warrantable to assume positively in a given case, even after negative results have been obtained from careful abdomino-rectal palpation, assisted by a sound in the bladder, that no traces of a uterus exist; for even upon the post-mortem table errors have arisen, and the rudiments of a bilobed uterus have been mistaken for the Fallopian tubes, or a hollow rudimentary uterus for the vagina.

Treatment.—No treatment will, of course, be of any avail.

II. Rudimentary Uterus: Uterus Rudimentarius.—*Anatomy.*—Between defectus uteri and uterus rudimentarius there is often no very great hiatus in the scale of development, for the more decided forms of the latter malformation may be almost indistinguishable from complete absence of the womb. Thus the presence of a slight indefinable thickening on the posterior surface of the bladder, or at the junction of the imperfectly developed broad ligaments, or again, of a solid, fibrous

mass, the size of a hazelnut, located at the point normally occupied by the womb, may be all that there is to indicate an attempt at uterine formation.

If development has proceeded a step farther, a solid, narrow, flat, laterally extended band composed of muscular tissue, with the tubes ascending and the round ligaments descending from it, may be encountered; or a fibrous mass without a neck, and solid, but still having the general conformation of the uterine body, has been observed, from the upper angles of which the round ligaments originate and extend downward into the inguinal canal.

In the uterus bipartitus, which exemplifies the next stage in progression toward the typical organ, two separate, round, solid, vertically placed bodies, composed of muscular and connective tissue, lie between the bladder and the rectum. Occasionally these two bodies unite toward their lower extremities, forming a mass not unlike the cervix in shape, which is in immediate relation below with a rudimentary vagina, while above they still remain independent, like two diverging horns, and are usually solid, but may present a slight hollow enlargement lined by mucous membrane at or near the point of origin of the round ligaments. To this latter abnormality the name uterus rudimentarius bicornis has been given, although some prefer the term uterus rudimentarius bipartitus.

With uterus rudimentarius, which is not confined to monstrosities, but occurs also in viable subjects, the external genitals, vagina, tubes, ovaries, and mammæ may exhibit the same variations in structure which have been alluded to in speaking of defectus uteri.

Etiology.—The cause which produces the rudimentary conditions just described operates during the very earliest stages of fœtal development, and as the exact time of its appearance and the degree of its activity vary, so a variation in results, though always within certain limits, will be observed.

In defectus uteri the elements from which the uterine body is to be formed are wanting or have been obliterated, but in the present instance they have appeared, but have been more or less destroyed, at divers periods of their development, by nutritive disturbances of differing intensities. It should not be forgotten, however, that there may be growth of even the lowest rudimentary forms.

Physiology and Symptoms.—Although in absence of the uterus and in atrophy of the organ the general conformation peculiar to the female and her desire for the opposite sex are preserved, yet there is such an imperfect development of other organs that the functions characteristic of woman do not come into play at all. The condition of the ovaries will determine the existence of ovulation. Menstrual molimina may, but menstruation cannot, occur, and vicarious hemorrhages are rare. Sexual intercourse is possible when the vagina is not too seriously involved, and even then the urethra may be utilized for this purpose. Conception is, of course, impossible.

Diagnosis.—It is not difficult to confound absence of the uterus with atrophy of the organ, when development has been arrested at a very early stage. Even on the most careful examination mistakes have been made by the most skilful among diagnosticians. In any doubtful case, to determine the presence or exact condition of the womb, the patient should be thoroughly anæsthetized, and the bladder and rectum should be empty. A sound or a silver catheter is introduced into the bladder, the finger of one hand is passed into the rectum, and the other hand is placed upon the abdomen; the entire length of the catheter or sound can now be felt between the hands if no uterus, or only an extremely rudimentary one, is present. Any solid mass lying in the median line between the rectum and the bladder is probably a rudimentary uterus. The tubes usually occupy a somewhat lateral position, but may be mistaken for uterine cornua. The ovaries, by their sharply defined boundaries, size, shape, mobility, and situation can be more or less easily recognized.

The more advanced forms of atrophic uterus are not difficult to map out, and, in any event, examination is often facilitated by palpation through the posterior bladder wall, if the urethra has been dilated by previous attempts at cohabitation.

Treatment.—If menstrual molimina occasion severe suffering, castration is a justifiable procedure. The rudimentary uterus has also been extirpated.

III. Absence or Atrophy of the Cervix Uteri: Defectus Cervicis Uteri et Cervix Uteri Rudimentaria.—*Anatomy.*—Numerous grades of this deformity may be encountered. The entire cervix is absent, or a solid fibrous mass or band replaces the normal structure. When its formation is more perfect the internal os is alone closed, or the external os may be thus affected, or both may be occluded, while the cervical canal between is partially or entirely patent. Atresia of the external os only, marks the slightest degree of this maldevelopment. The uterus above may be perfect in structure or rudimentary. The vagina is normally developed, though occasionally the upper part of the canal may participate in the cervical atresia.

Since obstruction is the essential accompaniment of absence or atrophy of the cervix, hæmatometra is the natural pathological sequence when menstruation occurs.

Etiology.—In the more pronounced types of the deformity under discussion, and especially if other portions of the genital canal participate in the existing maldevelopment, it is probable that there has been at best only an abortive attempt at cervical formation. But when the uterus, vagina, etc., are normal in structure and the cervix presents no very aggravated form of atresia, we must regard as the important etiological factor some

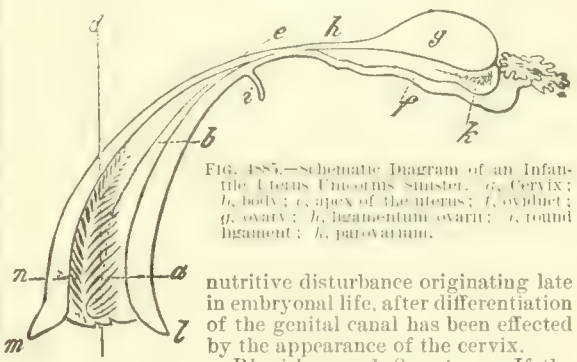


Fig. 1885.—Schematic Diagram of an Infantile Uterus Unicornis Sinister. *a*, Cervix; *b*, body; *c*, apex of the uterus; *f*, oviduct; *g*, ovary; *h*, ligamentum ovarii; *i*, round ligament; *k*, parovarium.

nutritive disturbance originating late in embryonal life, after differentiation of the genital canal has been effected by the appearance of the cervix.

Physiology and Symptoms.—If the ovaries and uterus are not arrested in development, menstruation will occur when puberty has been reached and hæmatometra appears, accompanied at first with menstrual molimina, and later by almost continuous pain, by pressure symptoms, and by threatened rupture of the Fallopian tubes. If the uterus and ovaries are rudimentary, there will be no menstruation, and therefore no blood stasis. Sterility is an invariable accompaniment of any form of cervical atresia.

Diagnosis.—Careful combined manipulation, performed as described in speaking of atrophy of the uterus, will reveal an absence or marked rudimentary condition of the cervix, while the failure to pass a sound or probe, or to find an opening in a neck apparently of normal structure, will at once denote the existence of one of the less marked forms of cervical atresia.

If hæmatometra exists, fluctuation can be detected through the rectum, and perhaps through the obstructing membrane, if it be not excessively thick and resistant, as is likely to be the case when the upper part of the vagina is involved in the atresia.

IV. The One-horned Uterus: Uterus Unicornis: Uterus Unicornis sine ullo Rudimento Cornu Alterius.—*Anatomy.*—When the uterus is one-horned the cervical is larger than the corporeal portion, and the latter consists of a long, tapering, arched, or bow-shaped

cone, situated laterally or lying obliquely in the pelvis, from the apex of which spring a Fallopian tube, a round ligament, and an ovarian ligament supporting an ovary.

In the purest form of this anomaly no trace of the other horn, or of the tube, round ligament, ovarian ligament, ovary, or broad ligament of the corresponding side is to be found.

Occasionally the one-horned uterus is solid.

Although uterus unicornis may be the only rudimentary condition discoverable in a given case, yet the vagina is often narrow, and in the more pronounced types of this anomaly one-half of the whole genito-urinary apparatus is occasionally found to have suffered in its development.

Etiology.—In uterus unicornis without a rudimentary second horn, it is probable that only one Müllerian duct has ever been formed.

Physiology and Symptoms.—Although the one-horned uterus differs in shape, size, and position from the normal uterus, yet when hollow it possesses such anatomical essentials as enable it to perform all the functions which pertain to that organ. Menstruation, conception, and pregnancy occur without hindrance, and even twins have been delivered from a one-horned womb. On account of somewhat deficient muscular development, it might be surmised that rupture of the uterus would be readily induced during the throes of labor. Such is not usually the case, although, if the muscular structure of the organ be weakened and displaced by the growth of placental vessels, such an accident during parturition is not improbable.

The muscular hypertrophy accompanying the first pregnancy assists the uterus unicornis in the part it has to play in those occurring subsequently.

Diagnosis.—Uterus unicornis is easily recognized on careful examination, a sound being introduced into the uterus and one examining finger into the rectum. Even when impregnated its shape and oblique position may be preserved; but the normal organ is not uncommonly deflected to the side at this period, and the one-horned uterus may be so broadened by the physiological hypertrophy of pregnancy as to lead to some confusion in diagnosis.

Treatment.—It is not unlikely that appropriate treatment will produce an enlargement and strengthening of the muscular structure of the one-horned uterus, and this is a very desirable end to be achieved when we consider the possible danger of rupture during parturition. When rupture at this period is threatened, labor should be expedited by artificial means, if necessary, and at the same time the risk of post-partum hemorrhage should be held in mind and proper contraction of the organ secured.

V. The One-horned Uterus with Atrophied Second Horn: Uterus Unicornis cum Cornu Rudimentario; Uterus Unicornis Excavatus cum Rudimento cornu Alterius Solido s. Excavato.—*Anatomy.*—On the convex side of an obliquely inclined uterus unicornis there may be found a rudimentary second horn, which exhibits in different cases various degrees of imperfect development. A solid muscular cord, or band, unconnected with the ovary above or the other horn below, is sometimes observed, but occasionally this is expanded at the upper extremity, is hollow, and communicates with the tube alone, or with the better developed cornu below, or with both, although it may be closed at each extremity.

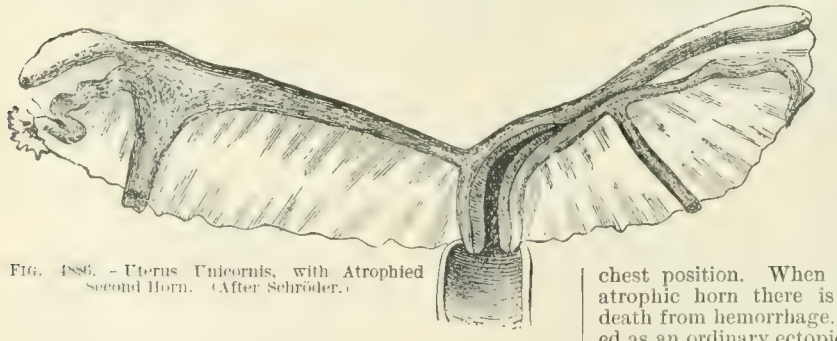


Fig. 4886. – Uterus Unicornis, with Atrophied Second Horn. (After Schröder.)

Etiology.—In this condition both Müllerian ducts have appeared, but one has been more affected in its development than the other by causes, of a nature already described, operating early in embryonal existence.

Physiology and Symptoms.—The functions which a rudimentary cornu attached to a one-horned uterus is capable of performing depend, of course, upon the degree of its development. If it is hollow and its inferior extremity is patent, menstruation may occur, though not so early nor in so great quantity as from the more perfect horn. But if there is no opening below, a slowly developing hæmatometra will result, and perhaps a hæmatosalpinx as well.

When pregnancy occurs, it is usually in the more typically formed cornu, and utero-gestation is quite normal, and parturition also, except when, as sometimes happens, the rudimentary horn offers a mechanical obstacle to its accomplishment.

It is quite possible, however, for the product of conception to be implanted in the rudimentary horn, especially if a communication exists between it and the vagina through the normal cornu. When there is no such communication, a like result may be accomplished by the processes known respectively as transmigratio ovuli externa and transmigratio seminis externa.

When pregnancy does take place in the atrophic horn, this enlarges up to a certain point and then ruptures, as a rule between the second and fifth months of utero-gestation, death usually ensuing, although encapsulation of the fœtus may occur and recovery take place. Still, pregnancy may go on to full term without interruption.

The normal horn participates to a certain extent in the changes incident to pregnancy, and a decidual membrane forms within its cavity.

Diagnosis.—The existence of a conical arched body, with a mass more or less like itself springing from its convex surface, will convince the examiner that he has to do with a one-horned uterus with a rudimentary second horn, although a pedunculated subperitoneal fibroid may closely resemble the atrophic cornu and be mistaken for it.

When pregnancy occurs in the poorly developed horn the symptoms will all be those of extra-uterine fœtation, and as the round ligament cannot be mapped out with any certainty, it will remain a matter of doubt whether the ovum has been implanted in the Fallopian tube or in the rudimentary horn.

Treatment.—In this condition active interference is indicated only when there has been considerable blood stasis in the rudimentary horn and rupture or other dangers threaten, or when the horn offers a mechanical impediment to delivery, or is itself the seat of pregnancy. Accumulated blood may be evacuated by trocar puncture through the vaginal vault, although in some cases laparotomy and drainage, or entire removal of the sac, will be the more judicious procedure.

The rudimentary cornu, which makes labor tedious or impossible, may be elevated above the parturient canal by vaginal manipulation combined with the assumption of the Sims or knee-chest position. When pregnancy occurs in a markedly atrophic horn there is serious danger of rupture and death from hemorrhage. The condition should be treated as an ordinary ectopic gestation should be, by abdominal section and removal.

VI. The Two-horned Uterus: Uterus Bicornis.—*Anatomy.*—Next above the uterus unicornis with a rudimentary subsidiary cornu, is placed, in the scale of

development, the uterus bicornis. Various degrees of this latter rudimentary condition are described. In the lowest and most imperfect forms there are two separate and distinct hollow uterine bodies, projecting laterally like horns, which unite below in a common cervix, deeply furrowed before and behind. Again, the union is more complete and a sulcus is found only on the external aspect of the fundus, indicating the point of coalescence of the two cornua, while the rest of the body and the cervix, though unusually broad, show no furrowing of their outer surfaces. This condition has been variously termed uterus arcuatus, uterus introrsum arcuatus, and saddle-shaped uterus. When the fundus shows no furrow, but is flat—the next step in advance—the designations uterus triangularis, uterus incudiformis, and uterus planifundalis have been employed. In all forms of the two-horned uterus one side of the organ is apt to be larger than the other, and the left horn—that is, the normally developed organ—lies a little farther forward than the right. A partition wall more or less complete may divide the cavity of the uterus bicornis. The entire womb may be thus separated into two parts (uterus bicornis septus), or the body is divided while the horns remain distinct (uterus bicornis unicorporeus), or the body is double and the cervix single (uterus bicornis unicollis). Still, in many cases no pronounced partition is discoverable, though bands of tissue may run from the anterior to the posterior uterine wall, or a prominent ridge on the interior of the uterus may show an attempt at division. With uterus bicornis, although the vagina is often found divided, the remaining elements of the genital system are usually perfect in development. Sometimes, very curious to say, the face, thorax, and pelvis are broadened, as if to correspond with the unnatural width of the uterus. When one-half of a two-horned uterus is conspicuously behind its fellow in development, it is not unusually occluded: this is more frequent on the right than on the left side, and the atresia may be seated in the cervix or at the external os uteri.

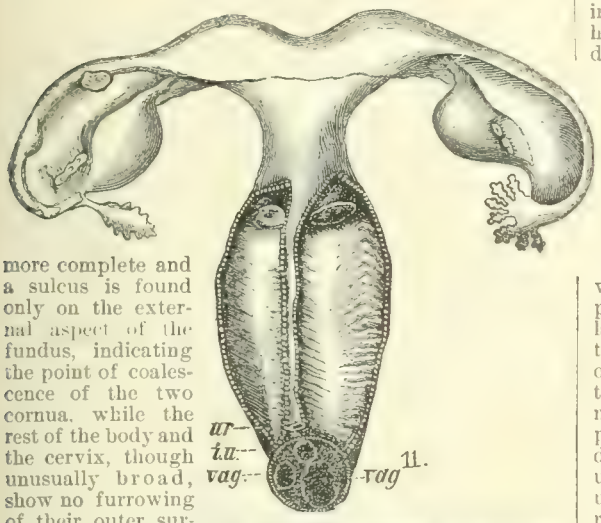


FIG. 4887.—Uterus Bicornis. (After Hunkemoller.) *ur*, Urethra; *i.u.* entrance to the urethra; *vag* and *vag'*, entrances to vagina. The anterior wall of both vaginæ has been removed.

Etiology.—When coalescence of the middle portions of the Müllerian ducts is only partial, uterus bicornis will result, and the degree of deformity will depend upon the extent of fusion. The recto-vesical ligament undoubtedly plays an important part in the genesis of this rudimentary condition. This ligament, as its name implies, stretches from the anterior surface of the rectum to the posterior surface of the bladder, and lies in the furrow on the fundus uteri. Its origin is somewhat doubtful. Winckel suggests, from a study of a case of his own, that its formation is due to an unfolding of the peritoneum before the upward-growing uterus. He examined the tissues of the ligament microscopically, but could find no muscular fibres.

Physiology and Symptoms.—The uterus bicornis may, in the performance of the functions pertaining to the normal womb, act like two independent organs. Thus, while menstruation may occur simultaneously from the two cornua, it is not unusual to see them alternately performing this function, and a periodical flow may continue to escape from one cavity after pregnancy has occurred in its fellow. If one side is occluded (bilateral atresia has never been observed), hydrometra or hæmatometra develops slowly, and here, as also with pyometra, rupture of the sac may take place and its contents be discharged into the vagina, into the better developed cornu, or into the abdominal cavity. Hæmatosalpinx is a frequent and early source of danger.

A considerable number of patients with two-horned uterus never conceive, but this is not due to the condition of the uterus, but rather to the fact that intercourse is carried on in the larger and occluded half of the accompanying divided vagina. Either half of a two-horned uterus may become gravid, the other horn participating in the subsequent hypertrophic and decidual changes. The fœtus may lie largely in one cornu while the placenta is adherent to the inner surface of the other. Sometimes pregnancy occurs first in one and then in the other horn, and in twin pregnancies, which are not uncommon, both ova may occupy the same or each a different cornu. The presentation varies largely with the grade of the rudimentary condition: in uterus bicornis septus and uterus bicornis unicollis, the vertex; with a common uterine cavity, the breech; in uterus arcuatus unicorporeus, transverse presentations are common. During labor, contractions may occur simultaneously in both horns of the uterus, or the empty horn may play an entirely passive part in the process of delivery. In twin births contractions of the two horns alternate, and delivery from one may be accomplished much earlier than from the other. Independence of action between the two cornua is observed most characteristically when independence of structure is most marked.

The course of utero-gestation and of the puerperium in individuals with uterus bicornis is usually uneventful, but labor is apt to be tedious, difficult, or dangerous. The non-gravid horn, the recto-vesical ligament, or the septum dividing uterus or vagina, may oppose barriers to the exit of the child which are difficult to surmount. Death from exhaustion is apt to ensue, and rupture of the lower uterine segment has been observed. In nearly every case some operative interference is called for to insure safe and rapid delivery. Placenta prævia is by no means uncommon, and post-partum hemorrhage is to be feared when the placenta is attached to the uterine septum.

Diagnosis.—When, from great breadth of the uterus or the presence of a divided vagina, uterus bicornis is suspected, a correct diagnosis is often arrived at by the introduction of two sounds into the womb. When their points cannot be approximated low down in the uterine cavity a partition is usually present, and if after further introduction they diverge markedly toward the respective sides of the pelvis, they have probably entered the independent cornua of a two-horned uterus. Diagnosis is facilitated also by the various combined methods of examination, and is especially easy when, after labor, the finger can be introduced through the dilated cervical canal.

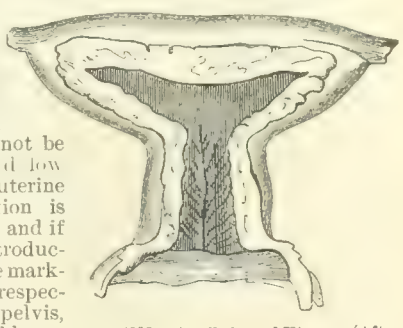


FIG. 4888.—Anvil-shaped Uterus. (After Oldham.)

Treatment.—The same rules governing the operation for the evacuation of fluid retained in the rudimentary cornu attached to a one-horned uterus, apply when a like result has followed unilateral atresia of a two-horned uterus, and the same complications originating in imperfect drainage and rupture of a tubal blood sac are to be feared. Puncture of the sac is best made at its most dependent part. Müller observes that when the head during delivery is impeded by the recto-vesical ligament, the correction of the obliquity of the pregnant horn, or placing the patient on the side corresponding to the non-pregnant half of the womb may suffice; but if not, podalic version and extraction should be attempted. Obstructing septa or bands may be pushed to one side or divided.

VII. The Two-chambered Uterus: Uterus Bilocularis; Uterus Septus, Subseptus, or Uterus Septus Duplex. —*Anatomy.*—The two-chambered uterus is an organ rather broader than normal, but of perfect outward form except that there is usually some disparity in size between the two sides. A partition more or less perfect divides its cavity into two lateral portions. If this dividing wall extends from the fundus downward only for a short distance into the body of the womb, we have the sub-variety of uterus bilocularis known as uterus bilocularis unicorporeus or uterus subseptus unicorporeus; if to the level of the internal os, the designation uterus bilocularis unicollis, or uterus subseptus unicollis is employed; if to the external os, uterus bilocularis septus sive completus; when the partition extends only so far into the cervical canal that there is but one external opening (os) common to both chambers, the condition is termed uterus subseptus uniforis. The name uterus biforis supra simplex indicates that a septum is situated only in the neighborhood of the external os and that the cavity above is single. Occasionally the uterine partition is continuous with a septum dividing the vagina into two lateral chambers. As in other varieties of duplex uterus, the dividing wall is not always perfect in its structure, but may contain one or more perforations. Atresia of one chamber has been observed but rarely.

Etiology.—As would be supposed, this malformation is referable to the same period of intra-uterine life as uterus bicornis, or perhaps, better, to a slightly later time in the same period. The causes of the two anomalies are the same. The fusion of the Müllerian ducts has been complete, but the partition wall has only partially disappeared, or else persists throughout.

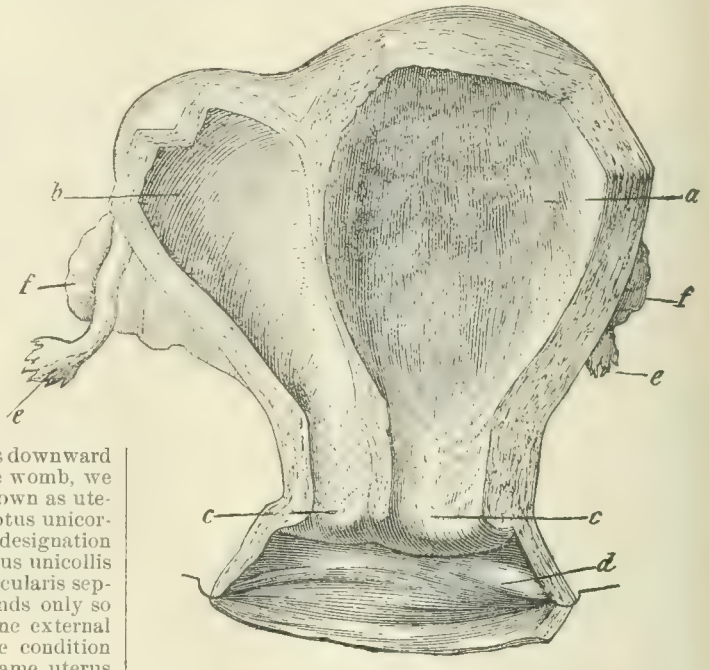


Fig. 4890.—The Same, Front View. Anterior walls removed.

Physiology and Symptoms.—The two-chambered uterus, in so far as menstruation, conception, pregnancy, and delivery are concerned, in no way differs from the two-horned uterus.

Diagnosis.—On bimanual examination the uterus is found to consist of a single, somewhat broadened body, while two sounds introduced into its interior are prevented from touching by the dividing wall. With all the facilities at our command it is safe to say that, in the living subject, it is not possible to differentiate the two-chambered uterus from the least rudimentary forms of the two-horned organ.

Treatment.—During labor, as in the uterus bicornis, the septum may interfere with the process of expulsion, and manual or instrumental assistance is occasionally required.

VIII. The Double Uterus: Uterus Didelphys: Uterus Duplex Separatus: Uterus Diductus.—*Anatomy.*—In non-viable monsters, and occasionally in subjects capable of life, two uteri are sometimes found quite distinct and independent of each other in all their parts, and separated, sometimes widely, by the recto-vesical ligament, urachus, bladder, and rectum. Each uterus is of a cylindrical or conical shape, is continuous above with a Fallopian tube, and terminates below in a cervix. The presence of other grave anomalous conditions shows that quite a severe blow has been struck during the progress of development. Thus the cervical portions may end in the bladder, rectum, or cloaca, or in the respective halves of a septate vagina, which themselves terminate in these cavities. The uteri also may be solid throughout or a limited atresia of either organ may be present.

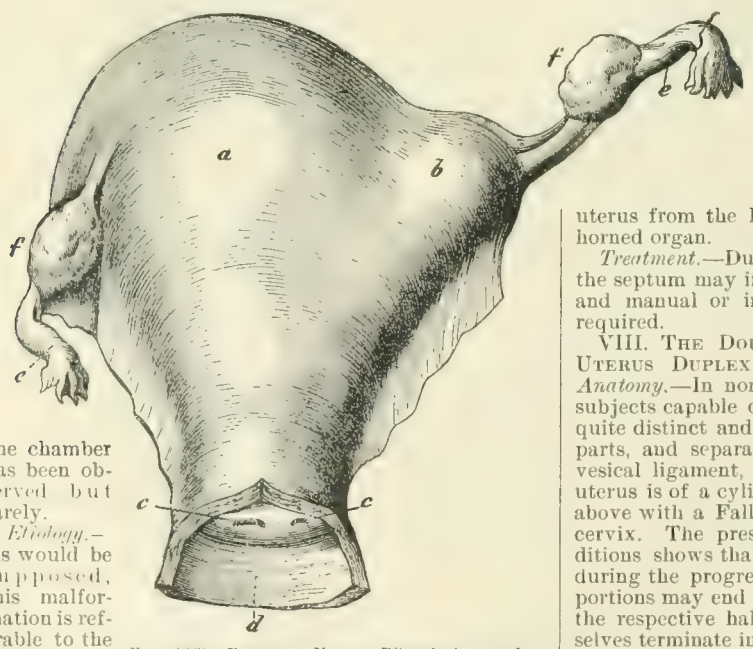


Fig. 4889.—Pregnant Uterus Bilocularis. (After Cruveilhier.) *a*, Right horn; *b*, left horn; *c*, external os; *d*, vagina; *e*, tubes; *f*, ovaries.

Etiology.—Before the eighth week of embryonal life, when as yet there has been no approximation or fusion of the Müllerian ducts, certain of the abdominal or pelvic organs among which are the bladder and intestine, force their way between the ducts and prevent their union. The recto-vesical ligament is also, no doubt, an important etiological factor. As a result of this interposition the formation of a single uterine body is rendered impossible.

Physiology and Symptoms.—In double uterus the menstrual discharge does not seem to alternate between the two cavities. Either may be occluded, and either organ or both simultaneously may become gravid.

Diagnosis.—In the recognition of the rudimentary condition under discussion, it has been truly said that the presence of two vaginal portions are of the utmost diagnostic value; for since the tubes which coalesce to form the middle portion of the genital tract unite from below upward, two cervices predicate two independent uterine bodies. If a sound is introduced into each uterine cavity, a finger inserted in the rectum can be pressed forward in a straight line without coming in contact with either uterus.

Treatment.—Retained menstrual blood is to be evacuated, and any obstacle offered to delivery is to be overcome by methods which have already been described.

IX. Faulty or Deficient Development of the Uterus: Hypoplasia Uteri.—*Anatomy.*—Under this head are grouped a large number of associated conditions, in all of which the uterus is fairly well developed, but has not quite reached the type of structure usually found in adults. Thus it may retain in later life the characteristics of the organ as found at the time of birth (uterus fœtalis), when the cervix is large and the body small, the whole possessing the shape of an anvil, while often an extreme degree of cervico-corporeal anteflexion exists. Again, it may be developed yet a little further, and though still unnaturally small, with thin walls, the body and cervix are of equal size, or the former is somewhat larger than the latter (uterus pubescens; congenital atrophy or hypoplasia of the uterus).

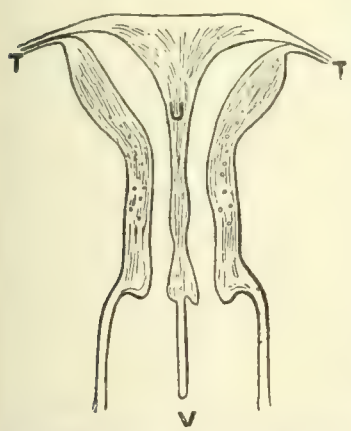


Fig. 4891. Bilocular Uterus and Vaginal Septum; Vertical Section. (Kussmaul.) *U.* Partition which divides the uterus into two halves; *T.* tubes; *V.* vagina divided by the uterine septum prolonged.

The walls are occasionally excessively thin and membranous (uterus membranaceus). The body and cervix may exhibit the same relative proportion to each other as in the perfectly developed uterus, but the whole organ perhaps is still deficient in size and possesses walls of abnormal thinness, while the plicæ palmatæ pass well up into the cavity of the corpus (uterus infantilis). All these forms are closely allied with one another, and with the least pronounced types of congenital malformation on the one hand and the normal adult uterus on the other. The term hypoplasia uteri may be used to include them all. As a rule, some of the remaining elements of the genital system show slight errors in development, and the ovaries are not infrequently rudimentary, or are sometimes entirely absent. The heart and the rest of the vascular apparatus may likewise be undeveloped.

Etiology.—Hypoplasia uteri cannot with justice be called a purely congenital condition. It is true that during the final months of embryonal life injurious influences, such as constricting peritoneal adhesions, may prevent a uterus almost completely formed from attaining anatomical perfection. But unhealthy systemic states (associated with disease of the vascular or nervous

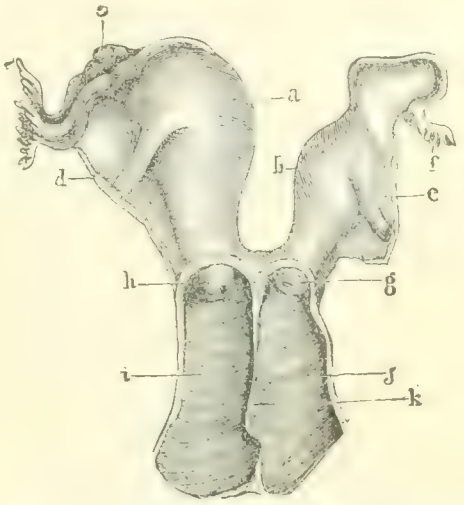


Fig. 4892.—Didelphic Uterus and Divided Vagina. (Olivier.) *a*, Right segment; *b*, left segment; *c*, *d*, right ovary and round ligament; *e*, *f*, left ovary and round ligament; *g*, *i*, left cervix and vagina; *h*, vaginal septum; *k*, right cervix and vagina.

system) during infancy or childhood, and lack of ovarian stimulation when these glands are absent or rudimentary, may bring about a like result.

Physiology and Symptoms.—It is the condition of the ovaries rather than that of the uterus which determines largely the nature and degree of the disturbances which accompany hypoplasia uteri. Menstruation may not appear at all, or may be scanty, irregular, and painful; and pregnancy, when it takes place, is not unlikely to end in abortion.

Diagnosis.—If, upon examination, the uterus is found to be less than two inches in length; if the cervix is larger than the body; and if the uterine walls are thin and membranous, even with a cavity which measures a little over two inches, the condition is one of hypoplasia; though we should be careful to exclude uterus unicornis before expressing a final opinion.

Prognosis.—In many cases a hypoplastic uterus will of itself, or in consequence of appropriate treatment, or of pregnancy, take on further growth, and ultimately attain normal proportions.

Treatment.—When the general condition is good; when the ovaries are present and are not excessively atrophic, and when the uterus is not too small, much can be done for the relief of amenorrhœa, or dysmenorrhœa with scanty menstruation, by the employment of the well-known local uterine irritants, and if these fail and suffering is excessive, castration in suitable cases should be resorted to.

Fig. 4893. Infantile Uterus. (Schröder.)

X. Slighter Developmental Anomalies of the Uterus.—1. *Obliquity of the Uterus; Obliquatus Uteri quoad Formam.*—From deficient development of one Müllerian duct, and from the traction exerted by a broad ligament shortened by fœtal inflammation, one side of the uterus may be somewhat smaller than the other, and the organ is thus made to occupy an oblique position in the pelvis (Fig. 4894).

Dysmenorrhœa and sterility usually accompany this condition.

2. *Congenital Ante-, Retro-, and Lateropositions of the Uterus.*—The uterus, although normally formed, may be situated too near the anterior, posterior, or lateral wall of the pelvis. If displaced laterally, it is usually toward

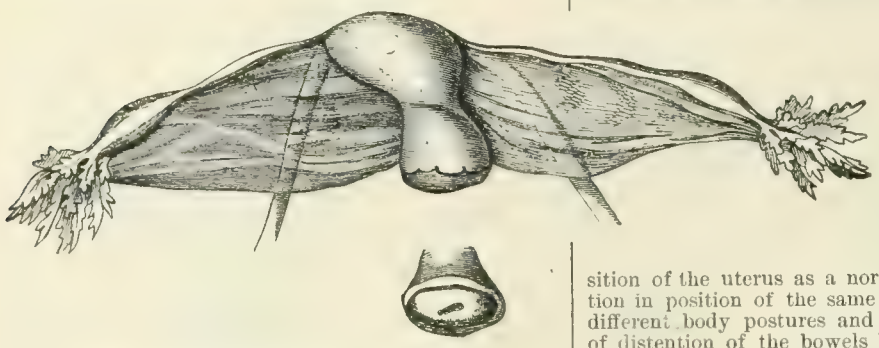


FIG. 4894.—Obliquity of the Uterus. (After Tiedemann.)

the left side. Contraction of one or the other broad ligament, and unusual size of neighboring organs, may bring about this result.

3. *The Double-mouthed Uterus: Uterus Biforis.*—An antero-posterior partition may divide the external os into two lateral halves, the cervix and uterus being otherwise normal in every particular. As in other forms of septate uterus, of which this represents the least pronounced type, the dividing band may offer an obstacle to the passage of the presenting fœtal extremity, and may, when ruptured, either cause considerable hemorrhage or form a starting-point for septic infection. If the septum during labor cannot be pushed aside, it can with safety be ligated in two portions and divided.

4. *Abnormal Plication of the Cervical Cavity.*—In this condition a fold of tissue, not unlike a second portio vaginalis, projects into the cervical canal, causing hemorrhages occasionally, and leading also to tedious labor. Incision or ablation is sometimes indicated.

5. *Abnormal Communications with the Uterus.*—The uterus may either open into the cloaca, or have faulty communications with different portions of the urinary system, or with the rectum. A case is on record in which one side of a uterus bipartitus opened upon the external surface of the body.

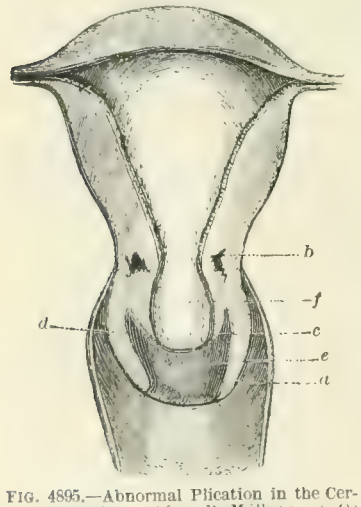


FIG. 4895.—Abnormal Plication in the Cervical Cavity. (After P. Müller.) *a*, Os externum; *b*, os internum; *c*, *d*, abnormal fold; *e*, *f*, cervical cavity.

6. *Premature Uterine Development.*—Along with the breasts and the organs peculiar to the female, the uterus is occasionally found precociously developed, and menstruation occurs prematurely.

7. *Hernia Uteri.*—The uterus, along with a prolapsed ovary, has been known to descend into a congenital inguinal hernial sac, and to become pregnant in this peculiar situation, Cæsarean section being thereby necessitated.

George Woodruff Johnston.

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UTERUS, DISEASES OF: DISPLACEMENTS.—A displacement of the uterus may be defined as a permanent departure from a normal position, and is therefore to be sharply distinguished from a temporary normal deviation. One reason for the slowness of investigators in the past to agree upon any position of the uterus as a normal one has been the variation in position of the same uterus when examined in different body postures and under different conditions of distention of the bowels by gas or fæces, or of the bladder by urine. In the perfectly normal pelvis the range of mobility is great, the condition being one of delicate poise maintained by the resultant of various forces, while the supporting structures are elastic, and some of them (round ligaments) are contractile.

Several structures more or less yielding and elastic serve to maintain the uterus in position. The upper portions of the broad ligaments at the sides and the round ligaments forward and laterally serve chiefly as stays or guys. Connective tissue in the lower portions of the broad ligaments, together with the so-called utero-sacral ligaments and bladder attachments in front, serves as a kind of sling attached low down on the organ, and gives support to its weight. The most important supporting structures are the muscles and fascia of the pelvic floor, chiefly the levator ani and coccygeus muscles, and the internal pelvic fascia with the perineal fascia (Fig. 4896). Another supporting influence may be likened to hydrostatic pressure. When the pelvic floor is intact, the tonicity of its muscles and of those of the abdominal wall serves to some extent to float, as it were, all movable bodies in the abdomen. This support is greatly reduced when the abdominal parietes have lost their normal tone.

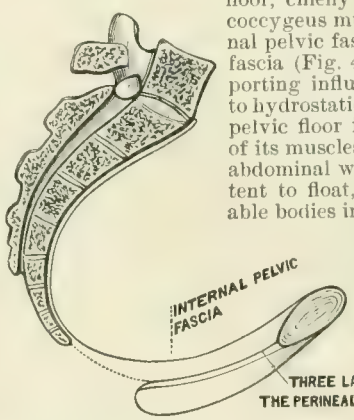

FIG. 4896.—Diagram showing Arrangement of Pelvic and Perineal Fasciæ. (Tarnier.)

The uterus moves with the whole pelvic diaphragm in the acts of vomiting, violent coughing, or straining in defecation. As it is attached to the bladder by a comparatively broad surface, the constantly varying distention of that organ swings the upper part of the uterus forward and backward. A range of normal mobility of several inches can be demonstrated without instrumental traction by contrasting the position of the cervix when the patient is in the standing position, with its position in the knee-chest posture after air distends the vagina. Under anæsthesia the cervix may with a tenaculum be drawn to the vaginal outlet without injury.

It must be understood that nearly all illustrations of the female pelvis are misleading, in that for the sake of clearness the vagina, bladder, and rectum are represented as distended, whereas the walls of the empty organs are in contact and occupy very little space.

The normal uterus is poised in the pelvis, the organs

being empty, the cervical portion almost central and as high as the top of the symphysis pubis, the fundus inclined forward almost horizontally and at times a little to the right or left to accommodate the rectum. The fundus is readily felt by the examining hand near the pubic bone, behind and below a line joining the promontory of the sacrum with the top of the symphysis (Fig. 4897).

Causes of Displacement.—Congenital defects of development result in some changes of position, chiefly backward deviation of the axis or a curving of the axis of the organ forward upon itself. These congenital alterations are usually accompanied by an imperfect development of ovaries and tubes, as well as of the uterus, though the external genitalia may be normal. The accompanying dysmenorrhœa and sterility are usually difficult to overcome.

Acquired displacements may be due to sudden strains, especially downward strains, to the slow action of tumor pressure, of gravity, of intra-abdominal pressure, or of contraction of inflammatory adhesions, while among contributing causes are laceration of the pelvic floor, subinvolution after labor, hyperplasia, œdema, passive congestion, general loss of muscular tone, faulty dress, constipation, infrequent emptying of bowel and bladder.

Sudden or acute displacements are usually backward and downward. They occur in persons who have sustained laceration or overdistention of the pelvic floor, though a few cases have been reported in which the cervix has appeared through the vulva in the virgin as the result of strain, and it is not very uncommon to have the fundus forced backward into acute retroversion in the unmarried. The history of the case usually shows that strain had been applied while the person was in an extreme stooping posture, as in lifting a heavy weight from the floor, or it may result from a fall upon the nates. One of the writer's patients, when a girl of fifteen years, previously perfectly well and totally unconscious of her anatomy, while lifting the corner of a heavy cook stove and trying to put a block under it, felt something "give way." Great pain in the lower pelvis and back followed, confining her to bed for a few days. There was soreness in walking, lasting months. The uterus remained in retroversion, and was an element in a disability which had continued for years until completely relieved by operation. Another patient, with a rather fat abdomen and an impaired pelvic floor, suffered acute retroversion while stooping and lifting the tray of a trunk. There were acute pain in the pelvis and back, frequent urination, and pain down the thighs. The uterus was caught below the promontory of the sacrum. Immediate relief followed the reduction of the displacement. In the extreme flexion of the thighs or the abdomen, not only is the muscular support of the perineum relaxed, but considerable pressure is made by the thighs upon the abdomen. The relief obtained in the squatting position, naturally assumed by some persons in extreme cases of difficult defecation, illustrates the mechanical principles involved. The uterus when suddenly forced down and back is most likely to be caught below the sacral promontory when the organ is somewhat enlarged by an early pregnancy or when the promontory projects well forward.

Laceration of the pelvic floor and imperfect involution after labor are the two chief elements in the production of *gradually acquired* displacements. The lacerations which occur during labor are not to be regarded as involving only the perineal body and the outlet of the vagina. A very complicated series of changes has taken place in the whole pelvic diaphragm. Planes of fascia are torn, and they slide one upon the other. Their attachments are pulled away, especially from the central areas. Great muscle planes are relaxed and torn apart, so that the levator ani, the coccygeus, and co-ordinating structures act less perfectly as a sling for the support of the pelvic viscera. If the upright position is resumed too early after confinement, and if the patient takes too little rest, not only the uterus but all the pelvic tissues fail to regain their normal tone. The uterus remains soft, large, and flaccid, and under the mechanical influence of gravity and imperfect support an exceedingly complicated change of relation of parts follows, infinitely varied according to the integrity of the holding power of untorn parts; but the uterus tends slowly to descend, tilting backward as an early step; the vaginal walls, becoming lax and redundant, are protruded before the descending

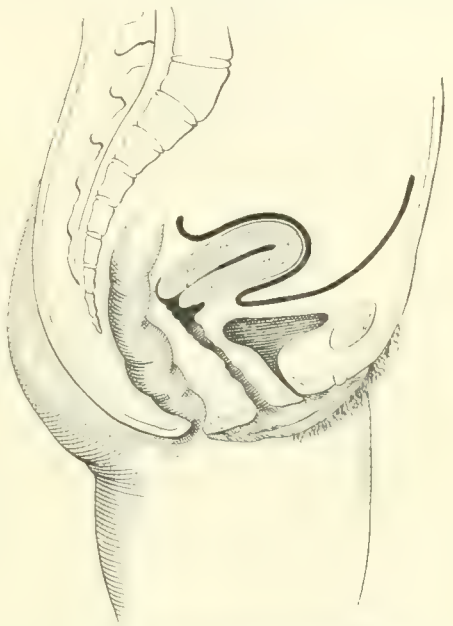

Fig. 4897. Normal Position of the Uterus.

bladder and rectum, until in extreme cases a true hernia of pelvic contents and even small intestine takes place through the pelvic outlet.

The *contraction of adhesions* which result from inflammatory disease in the abdomen, is responsible for some well-marked uterine displacements, especially those in a backward and those in a lateral direction. When, for example, a collection of pus, two or three inches in diameter, forms behind the uterus and broad ligaments, a heavy wall of plastic exudate unites the uterus and upper edges of the broad ligaments to the large intestine behind or to both large and small intestines, the omentum still further covering in the mass. Should this pus escape into the bowel or bladder or by the slow process of absorption disappear, the limiting wall of adhesions, following the shrinkage, slowly contracts around the remains of the mass. This contraction will in some cases fix the uterus and tubes, pulling the former slowly back over the disappearing pus sac. The influence of other causes which have been mentioned is obvious without detailed description.

Varieties.—The varieties to be described are: Upward, lateral, forward, backward, and downward; the organ may also occupy various hernial sacs, or may be completely turned inside out, the so-called inversion.

Upward displacement of the uterus is seen only as the result of the growth of tumors. A dermoid cyst of the ovary for example, or a nodule of a fibroma of the uterus, may become adherent in the pelvis behind the uterus, and by its growth push that organ out of the pelvic cavity entirely. Uterine fibromas which completely surround the uterus, grow too large for the pelvic cavity, and drag the uterus and bladder upward, stretching the vagina, so that on examination the os uteri is found to be completely beyond the reach of the finger. The treatment is determined by ordinary surgical principles in the removal of the growths, should that be called for.

Lateral displacement may follow contraction of plastic exudate or adhesions about an obliterated pelvic abscess.

especially in the broad ligament or peri-uterine connective tissue. The writer has seen the uterine cornu attached hard and fast to the bony pelvis at the side from such a cause. The abscess had been drained above

FIG. 4898. Anteflexion of the Uterus.

Poupart's ligament several years before. Broad-ligament cysts and intraligamentary uterine fibromata crowd the uterus to one side. No symptoms are directly caused by these forms of displacement.

Displacement Forward; Anteversion. — Twenty-five years ago the inclination of the axis of the uterus well forward (anteversion) was considered to be pathological by many gynecologists, and much ingenuity was expended upon the mechanical correction of the supposed resulting disabilities, including sterility, frequent urination, and dysmenorrhœa, by pessaries or by operations on the cervix or vagina. As the result of further observation opinion has changed, so that treatment is now no longer directed to this condition, and the object of the numerous operations is to induce the uterus to stay forward in what is now considered the normal position.

Anteflexion, however, when of extreme degree is recognized as pathological. This involves a bending or curving forward of the uterine axis. It is frequently found in an infantile or undeveloped uterus, associated with scanty, painful menstruation and sterility in persons of neurotic tendencies (Fig. 4898). Much discussion has arisen as to the rôle played by the flexion in the production of pains and sterility. It is claimed with truth that there is no real obstacle presented to the passage of menstrual blood or of spermatozoa unless the uterine canal is sharply bent at an angle. A gradual curve, no matter how short its radius, does not affect the lumen of the uterine canal. Above a sharp angle, however, clots may form, and as they enlarge they produce a valve-like closure at the point of flexion. A point of great tenderness may at times be detected by the sound at the angle. One theory is that increased vascular tension induces painful pressure at this point. Where the endometrium is swollen or diseased, as evidenced by tenderness and abnormal discharges, benefit in a few cases may be obtained by a cautious dilatation and curetting of the uterine cavity, followed by packing of the canal, for twenty-four or forty-eight hours, with sterile or iodoformized gauze to maintain the dilatation; or, according to a few authorities, a stem pessary may be introduced to secure the healing of the parts in a more normal direction. Such methods require care and good judgment, as salpingitis or endometritis may be readily caused. Prevailing opinion is against the protracted wearing of stem pessaries, because of their dangerous pressure or irritation as foreign bodies. If the ovaries and tubes, as well as the uterus, are of sufficient development to allow pregnancy to occur, the conditions are usually greatly improved after labor and the subsequent involution of the parts. In many cases of undersized flexed uterus, the only benefit to be secured is through general tonic and roborant treatment directed to the improvement of the impaired nutrition of the nervous system, which is apt to be present. When the uterus is quite small, it does not develop under physiological stimuli and the sterility is permanent.

COMBINATION OF VARIETIES.—An abnormal curvature may accompany an abnormal position. For example, anteflexion may be combined with retroversion (Fig. 4899).

When the uterine canal remains straight, the backward change of direction of the whole organ beyond the perpendicular line of the body constitutes a *retroversion* (Fig. 4900). When the canal is curved backward by a bend in the body of the organ, the condition is known as *retroflexion* (Fig. 4901). The two conditions are very commonly combined, constituting the most important of the series of displacements, except downward displacements. The degrees of malposition are sometimes divided into groups, called first, second, and third, though their limits are arbitrary and of little practical value.

Retroversion and retroflexion may be considered together, as clinically their symptomatology and treatment are much the same.

Retroversion of a small healthy uterus which has not descended, occurring in a woman who has an intact pelvic floor and healthy ovaries and uterine tubes, may not cause any symptoms. Such a state of affairs would not call for treatment were it discovered. In almost all cases,

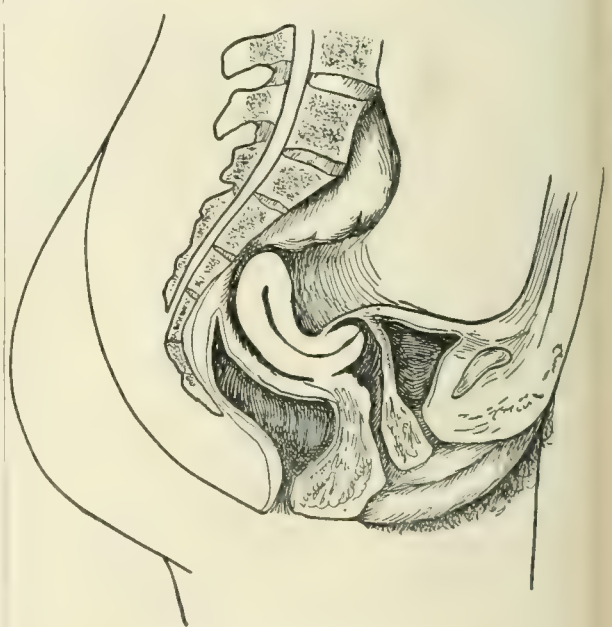

FIG. 4899.—Anteflexion with Retroversion.

however, the backward uterine displacement appears as a feature in a more or less complicated situation, which includes lacerated pelvic floor, prolapse of ovaries and tubes, possibly with adhesions, uterine descent, engorgement of pelvic vessels, subinvolution, endometritis, pelvic peritonitis.

Symptoms.—The symptoms of backache, bearing down, irritable bladder, increased duration and quantity with lessened interval of menstrual flow, are frequent. Occasionally patients complain of interference with defeca-

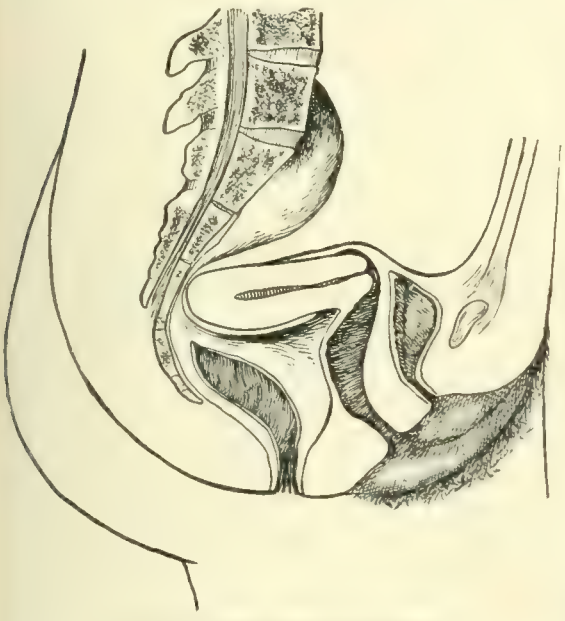

FIG. 4900.—Retroversion of the Uterus.

tion, and while lack of expulsive force, due to laxity of the pelvic floor, is most apt to cause the symptom, there seem to be a few cases in which the retroposed fundus does act as a partial obstruction to the onward passage of the contents of the rectum. Not all of these symptoms may be due to the retroversion, but the condition cannot be cured if this is not corrected. Indeed it must be constantly borne in mind, in considering all forms of uterine displacement, that it is frequently the conditions which accompany these disorders which give rise to symptoms and not the change in position or of curvature considered by itself.

Diagnosis.—The diagnosis is made by locating the relative position of the uterine fundus and of the cervix by means of the two hands, one pressing down the lower abdominal walls, while one or two fingers of the other are introduced into the vagina with firm backward and inward pressure. When the abdominal walls are rigid or the parts small, an anæsthetic may be required. It may be necessary to draw the whole uterine body downward by a tenaculum hooked into the cervix. It is unnecessary and often dangerous to introduce the uterine sound for purposes of diagnosis.

Replacement.—The use of a uterine sound or a jointed rod repositor within the uterus is to be condemned as likely to work mechanical injury, especially where peritoneal adhesions exist, and because a very early pregnancy cannot be excluded. By drawing down the cervix with a tenaculum, and carefully picking up the fundus with the hand applied to the abdomen, at the same time that the cervix is swung backward and inward, any non-adherent retroverted uterus can, with a little patience, be brought forward, although the manipulation may require some skill and practice. Until this replacement has been carried out, it is difficult and frequently impossible to determine with accuracy the condition of the prolapsed ovaries and tubes. When there are no peritoneal adhesions binding down the fundus, or when the median portions of the tubes and broad ligaments are free, the replacement of the uterus can be completely effected. Attention must then be turned to the problem, frequently a complicated one, of maintaining the organ permanently in a forward position. Lacerations of the pelvic floor must be repaired as a preliminary step, whether the mechanical support of a pessary is to be used or not. If it be decided not to use a pessary, various operations may be considered.

Prognosis.—Permanent cure may in a small percentage of cases be secured by repeated reduction and systematic massage, but the method is uncertain and open to objection. After the correction of constipation by laxatives, of uterine hyperplasia and pelvic congestion by hot douches, rest, medicated tampons containing especially ichthyol and boroglyceride, the use of some form of pessary may be considered. This instrument is far less frequently used than formerly, and there are many gynecologists who seldom or never make use of a pessary. Nevertheless, in the hands of a careful physician, of good mechanical judgment, this instrument may be made to give much comfort to a certain number of patients; it may even effect a cure in a few cases, especially those suffering from subinvolution after childbirth when only a few months have intervened since the labor.

The prognosis is good in all pathological forms of uterine displacement, if treatment is extended to the removal of causes, to the correction of concurrent conditions like endometritis and uterine hyperplasia, and if operations be carried out upon sound mechanical principles. Very many operations have, however, proved disappointing in their ultimate results, or they have, by interfering with pregnancy or with the normal mobility of the parts or by inducing a hernia, proved worse than the conditions which they were designed to correct. Moreover, a perfectly aseptic technique in operating is essential, for an operation correctly designed may fail to cure because of infection of the wound. This applies particularly to operations for shortening the round ligaments and to that which is designed to effect a suspension of the uterus, to be hereafter described. In both these instances infection may be followed by disastrous results, which leave the patient in a worse state than before.

Pessaries for the correction of anteversion are seldom required, and have gone almost entirely out of use. For posterior displacements the most useful form of pessary

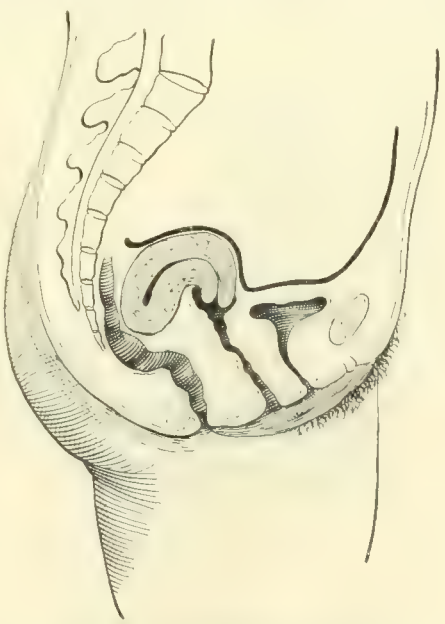

FIG. 4901.—Retroflexion of the Uterus.

belongs to the type represented by that known as the Smith-Hodge, which consists of a hard-rubber ring, flattened at the sides and with a double curve, the upper and posterior extremities being designed to hold the fun-

dus forward and at the same time draw the cervix backward (Fig. 4902). The anterior end is curved downward slightly so as to avoid pressure on the urethra. In conditions of great relaxation of the parts, a plain ring of soft rubber is occasionally used, but much greater irritation is produced by it than by the hard rubber instrument. Much ingenuity has been expended upon the mechanical support of the uterus, and the number of instruments suggested is very great. Very few of them, however, have acquired a permanent place in the treatment of the conditions for which they were designed, and a description of the numerous varieties will not be here attempted. When the causes which produced the original displacement can be removed by operation, the results are usually much more satisfactory, as the wearing of any instrument is a continual source of irritation, and more or less constant supervision by the physician is required. In particular, all forms of instrument which obtain the necessary support from external straps are unsatisfactory and in many cases injurious.

Stem Pessaries.—Many attempts have been made, by the use of an intra-uterine stem having the curve of a normal uterine canal, to correct flexions of the uterus. While it is possible, after complete dilatation and under aseptic conditions, for the uterus to tolerate such a foreign body, the dangers of endometritis, salpingitis, or other results from irritation have led to the abandonment of the instrument by the majority of gynecologists. The theoretical advantages are more than offset by the injurious results which have followed its use in some cases. If they are used at all, abundant provision must be made for the drainage of the normal secretions of the part. When any form of pessary is worn, a daily cleansing douche is required, and at least once a month the instrument must be removed by the physician and the effects of injurious pressure looked for.

Among the chief *causes of failure* in the use of instruments for the correction of uterine displacements, the greatest is the presence of inflammatory adhesions, either of the uterus itself, which may be thus confined in its abnormal position, or of the ovaries, broad ligaments, and Fallopian tubes. Retroversion especially is very commonly accompanied by salpingitis, metritis, or endometritis; and salpingitis is usually the more important disorder of the two. After the acute stages of tubal in-

Fig. 4902. Smith-Hodge Pessary in Position.

flammation have entirely passed, and after all exudates have been absorbed or organized, the resulting adhesions of previously smooth peritoneal surfaces are often firmly established and remain as a permanent condition. Strong fibrous bands and layers of newly formed tissue of great strength surround the parts in their new position, interfere with the return circulation, and prevent the normal change of position which is required as the rectum or bladder fills and empties, or as the person moves about, coughs, sneezes, and the like. The appendix may be caught and pinned down within this area of chronic peritoneal inflammation, and at the same time small masses of cheesy pus in the tubes or lower peritoneal cavity serve as a focus for succeeding attacks, which continue indefinitely the disability. Expert knowledge and skill are required to recognize and properly appreciate many of the conditions referred to, while even under an anæsthetic adhesions of the pelvic viscera, if in the form of long bands, will often escape detection. It may be regarded as axiomatic that the replacement of the uterus, even if possible, will not produce relief of symptoms in the presence of adhesions or inflammation of tubes, ovaries, and broad ligaments. Inasmuch as the uterus has a tendency, when its position is altered by a force from without, to return to its original position, the elastic pressure exerted upon the pessary used will be likely to produce injurious results. And then, on the other hand, if the normal position be maintained, pressure and traction upon the diseased tissues near by will ultimately increase the distress of the patient. An uncomplicated backward displacement of the uterus, for example, is a comparatively rare condition, and, like other displacements, were it not accompanied by increase in the size of the organ, endometritis, salpingitis, chronic peritonitis, pelvic congestion, varicose veins of the broad ligament, and imperfect circulation in lymph channels, it would produce comparatively little disability. While, therefore, a displacement of the uterus may be the most easily demonstrated feature in a given case, it cannot be too strongly urged that attention must first be given to the correction of complicating conditions, and especially to the removal of all adhesions, before the replacement of the uterus by any form of support is to be undertaken. This preparatory treatment may occupy weeks, and may consist of hot douches, of elastic packing in the knee-chest position, of the application of absorbifacients on carefully placed vaginal tampons, as well as of the correction of unhygienic conditions of all sorts. In the event of failure of these efforts abdominal or vaginal section may even be required, especially where destructive tubal inflammation has occurred. Rapid replacement of the uterus under anæsthesia has been advocated in some cases, for example by Schultze. This should be attempted only in simple cases, and by one familiar with intra-abdominal operating, as it is easy to rekindle a slumbering pelvic peritonitis, produce hemorrhage by laceration, or distribute the infected contents of a tube. If undertaken, the operation should be done only by the hands, *i.e.*, by using bimanual manipulations, while the cervix may be steadied or moved in the proper direction with a tenaculum. Replacement by means of an intra-uterine instrument with a mechanical arrangement for changing the direction of its outer extremity is open to the objection that it may perforate the uterus or otherwise injure it, and that, when a difficulty of one kind or another is encountered, cautious intelligent action is impossible.

Downward Displacements.—The downward are usually combined with the backward displacements, and are those which carry in their train the greatest amount of physical discomfort, disability, and in some cases secondary disease. The degree may vary from a trifling descent of all the structures in the pelvic canal, including the uterus, to the complete extrusion of the organ from the body (Fig. 4903). The uterus in its descent is usually accompanied by the bladder and the anterior wall of the rectum, which undergo stretching, the walls of the vagina are also stretched, as are the connective tissues and the fascial supports of the pelvic floor. In the greater degrees of downward displacement, known as procidentia uteri, very elaborate changes of structure and of anatomical relations have taken place, and cases vary greatly in the individual changes of relation which have occurred. Sometimes the uterine body escapes from the pelvic outlet and the fundus may be defined in the upper portion

of the protruding mass, while no great change has occurred in the size or shape of the uterus or of its cervical segment. In these rare cases the protruding mass forms a true hernia. A considerable portion of the bladder,

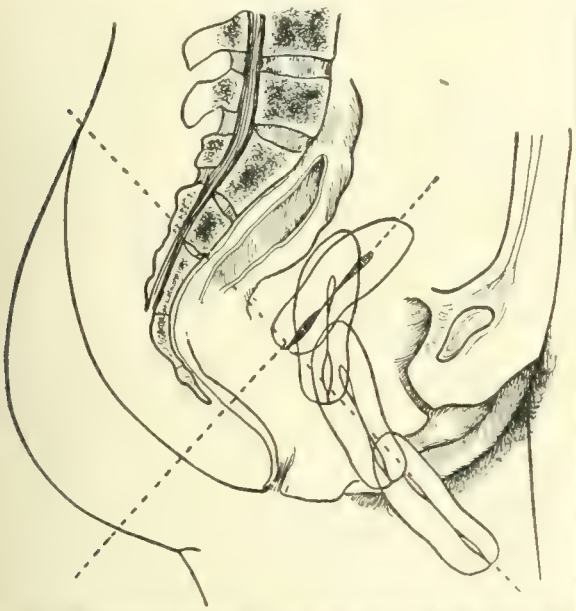

FIG. 4903. Prolapse of Uterus. Diagram represents the degrees of prolapse, but not the usual distortion of the organ.

all of its base, all of the vaginal walls and urethra, the lower portions of the broad ligaments, part of the uterine tubes, several inches of rectal wall, the ovaries, with some small intestine or omentum, may be found in the mass. More frequently the fundus of the uterus remains in the lower portion of the pelvic outlet together with the tubes and the ovaries, while the central and cervical portions of the uterine body elongate downward and undergo hypertrophy (Fig. 4904). The result is a very great increase in the size and weight of the uterus, its canal measuring six or eight inches in length, and the cervical segment may be two or three inches in breadth. Hypertrophy of the vaginal mucous membrane and underlying connective tissue and passive congestion and œdema unite in the production of an external mass which may be five inches in diameter. In some instances urination can take place only after the protrusion has been manually replaced and the urethral canal thereby unbent. Secondary changes due to chafing and passive congestion may produce superficial inflammation and ulceration, so that more or less bleeding is quite common, even in cases which are seen in old age and which have not undergone cancerous degeneration. The imperfect emptying of the bladder may result in decomposition of residual urine and secondary bladder or kidney changes. Defecation is more or less interfered with and frequently requires manual assistance; impairment of the return flow of blood favors the development of hemorrhoidal conditions and other disorders of the rectum. Notwithstanding the enormous amount of displacement and distortion of the parts, patients, especially working women of the phlegmatic type, will sometimes complain of surprisingly little discomfort, and many women, supporting the parts with a tight napkin, will perform heavy manual labor and entirely refuse operative relief. In the extreme degrees of downward displacement, no form of instrument or apparatus proves satisfactory, as anything which gives sufficient support is more than likely to produce irritation or ulceration from direct pressure. It appears impossible to secure in the greatly widened and straightened pelvic outlet a proper point of support for any instrument. In the minor degrees of this condition relief may be obtained sometimes for long periods by the use of the plain ring pessary, though each case requires an adaptation of the support to its peculiar conditions.

The operative relief of downward displacement has received much study, and many procedures have on protracted trial proved unsatisfactory. Removal of the uterus, occasionally advocated, does not restore the accompanying displacement of bladder, rectum, and vagina, and in well-marked cases of procidentia it has proved entirely unsatisfactory, unless followed by extensive plastic operations for the correction of the other elements in the condition and for the support of the other organs of the pelvis. Those procedures ultimately fail which do not succeed in restoring, to a large extent, the mechanical arrangement of supporting structures which originally maintained the uterus in position. All operations should aim at a restoration of the integrity of the pelvic floor, and particularly at repair of the torn fasciæ and separated fibres of the levator ani muscle. In addition to this the increased weight of the uterus must be corrected, its cervical segment, if elongated, must be shortened, and the utero-sacral attachments must be in effect restored in order to draw the cervix backward; and at the same time some operation must be carried out which will not only restore the normal forward position of the fundus, but will also, if possible, contribute to its support. In long-standing cases of procidentia the endometrium is usually diseased and hypertrophic glandular endometritis is commonly present. The first procedure to be undertaken, therefore, is curetting of the uterine cavity, and next the cervix is to be repaired if lacerated, or, if it is greatly elongated, the bladder and rectum are to be dissected off, the lateral blood supply of the uterus is to be ligated as in the early steps of a vaginal hysterectomy, and the lower portion of the uterus is to be amputated at such a point as will leave the organ approximately normal in length. This lessens the blood supply of the organ and tends to produce involution. When now the anterior and posterior flaps of the vagina are united to the flaps of the cervix by deeply placed radiating sutures, the deficient utero-sacral support is in effect supplied posteriorly, and the vagina and bladder are attached at a higher point on the anterior face of the uterus. An operation must now be performed that will diminish the cystocele. According to some methods a horseshoe-shaped denudation is made on the anterior vaginal wall and the edges of the denuded areas are united by rows of interrupted sutures. A preferable method includes free dissection of the anterior vaginal wall and its underlying connective tissue from the bladder over a triangular area whose base is directed toward the cervix, and whose width is determined by the degree of relaxation of the parts. The triangular flaps thus formed to the right and left of a median longitudinal incision on the most prominent portion of the cystocele are freely cut away; after which a series of buried superimposed catgut sutures is introduced to close the wound, and a superficial layer of continuous silk suture unites the cut edges of the mucous membrane and of the fascia beneath. This operation restores, better than can be accomplished in any other way, the integrity of the structures which normally support the bladder and anterior wall of the vagina.

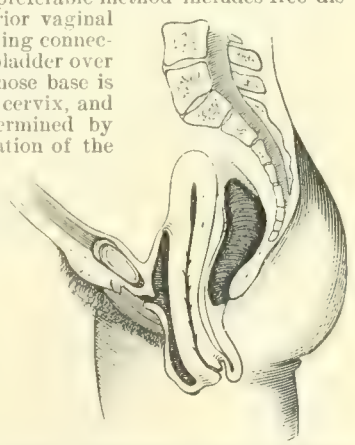

FIG. 4904. Procidentia Uteri. Hypertrophy of supravaginal portion of cervix.

Attention is now turned to the defective posterior wall, which should be widely denuded, the upper edge of the denuded area being continued at the sides higher than in the median line, as in the operation for restoration of the pelvic floor designed by Dr. Thomas Addis Emmet. The sutures are so introduced as not only to approximate the sides of the denuded area, but also to draw upward the prolapsed tissues. They take their point of support in untorn fascia at the sides of the pelvis. Another excellent plan of perineal repair is that of Hegar.

Any existing hemorrhoids should be removed by ligation or by cauterization. Extreme degrees of uterine descent will not be permanently cured unless, in addition to the procedures described, some operation be undertaken above the pubic bone to support the uterus and secure for it a permanent anterior direction. The operations that are most favored at the present time for securing these objects are either shortening of the round ligaments of the uterus, or an attachment of the fundus to the anterior abdominal wall.

Shortening of the Round Ligaments; also known as *Alexander's Operation.*—These cords of unstriped muscular fibre take their origin near the uterine cornu, pass forward and outward through a fold in the broad ligament, and entering the inguinal canal are attached at the external abdominal ring to its pillars and to neighboring tendinous structures immediately about the pubic spine. The ligaments may be pulled outward through the inguinal canal after their outer ends have been reached through a small incision over the external abdominal ring. The redundant portion having been cut away or attached by various methods to neighboring structures, the remaining portion of the ligament is sutured in the lower end of the canal. By some operators the round ligament is reached after an extensive opening of the inguinal canal, afterward shortened, and its remaining end attached. Other methods involve the opening of the abdomen in the median line, the folding and suturing of the round ligaments upon themselves, or to the uterine body, after the manner described by Matthew D. Mann, W. Gill Wylie, Palmer Dudley, and others (Fig. 4905). A plan has also been proposed for carrying a loop of round ligament, or the cut end back through a perforation made in the broad ligament to a point behind the uterus where it is to be sutured. The methods of intra-abdominal shortening of the round ligament have not been so extensively practised as those in which it is approached by way of the inguinal canal.

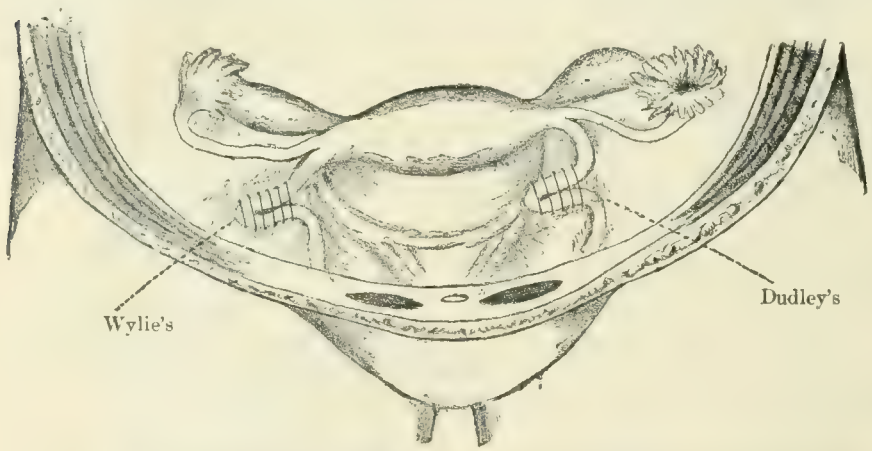

FIG. 4905.—Diagram of Wylie's and Dudley's Methods of Intra-abdominal Shortening of Round Ligaments.

Suspension of the Uterus.—In retroversion of marked degree, after adhesions or disease of tubes and ovaries have been appropriately treated, and after the problem of the support of the uterus from below has been met, the operation of uterine suspension, as devised by Howard Kelly, may be carried out. The object is not to hang up the uterus by a strong supporting band, but to form a light attachment of the fundus to the anterior abdominal wall, which elongates under subsequent traction and forms a delicate cord. This serves to maintain the uterus in the normal position of anteversion, so that the weight of the abdominal contents is received on the posterior instead of the anterior surface of the organ, and the mechanical forces of the normal uterine support are again put in play. The attachment is made by two or more sutures of fine silk entering the uterine substance a short distance posteriorly to the line of the tubes, emerging at a distance of about one-half inch, being again introduced on the peritoneal surface of the anterior abdominal wall, passing through the properitoneal fat, grasping a few fibres of the rectus muscle, crossing the wound and penetrating in turn rectus fibres, properitoneal fat, and fascia, again appearing through the peritoneum, when they may be tied within the peritoneal cavity and remain buried. The abdominal wound is closed separately in layers or by methods usual in the practice of the operator.

Objection is frequently made to this operation on account of its supposed interference with subsequent pregnancy. There have been reported a number of cases in which this operation had been performed, and in which formidable complications were met during labor. Such complications may usually be traced to a too great amount of fixation of the uterus at the original operation, or to inflammatory adhesions which have produced a firm attachment of the uterus to the abdominal wall. Such an attachment is not contemplated in the operation of uterine suspension, and should never be carried out in women who are liable to bear children. In the operations for the cure of procidentia in elderly women a firm attachment may, however, be made by an operation known as uterine fixation.

Fixation of the Uterus.—Through an abdominal incision in the median line just above the pubis, Olshausen secured the indirect support of the uterus by uniting the round ligaments and the broad ligaments to the parietal peritoneum on either side. He secured this union by means of buried sutures. Theoretically the operation provides an opportunity for hernia of the intestine between the fundus and the abdominal wall, and consequently it has never been widely practised. Leopold directly fixed the uterus by its anterior surface to the abdominal parietes after scarification. He passed three of the sutures which were destined to close the abdominal incision though the uterine tissue, one penetrating the uterus in the line of the tubes, another opposite the origins of the round ligaments, and a third still farther down the anterior wall. The result of this procedure was, as a rule, a very firm attachment of the uterus forward and above the bladder, especially when any appreciable degree of inflammatory reaction followed the operation. So firm is the attachment secured by this operation that pregnancy, should it occur, is likely to be followed by dangerous complications. In a number of instances complications of this nature have compelled a resort to the operation of Cæsarean section. It has been found, in these cases, that the anterior wall of the uterus develops as a thick compact mass, confined by adhesions to the brim of the pelvis, while the posterior wall of the uterus, stretching up-

ward, becomes greatly thinned; in consequence of which conditions the normal presentation of the child is rendered impossible, the engagement of the head does not occur, and even version or the high application of the forceps may fail to effect delivery.

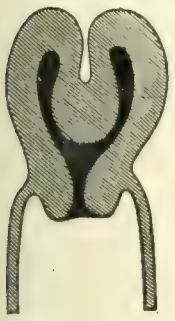

FIG. 4906. — Partial Inversion. (Thomas.)

Vaginal Fixation of the Uterus.— One of the three chief methods of securing the uterus in a forward position and of counteracting its abnormal descent is the operation known as vaginal fixation, which was elaborated by Mackenrodt, who described it in 1892, and by Dührssen, who worked along similar lines. In these operations an attempt is made to overcome the relaxation of the anterior attachments of the uterus, to attach the over-stretched vaginal supports at a higher point on the anterior surface of the uterus, and to overcome the downward displacement of the bladder. In performing the operation the lower limit of the bladder in front of the uterine cervix is first established, and then the surgeon proceeds to take the following steps: a transverse incision is made (just below the point fixed as representing the lower limit of the bladder) down to the bladder wall, and a longitudinal incision from the centre of this transverse line is carried forward nearly to the external urethral orifice; triangular flaps are made on either side and the bladder is separated from the vaginal wall and the anterior face of the uterus. The utero-vesical pouch of peritoneum is opened, any existing adhesions are separated, and the uterus is brought forward to its normal position and sutured to the cut edges of the vaginal wall. In order to overcome the objection that the changes effected by this operation interfere too seriously with pregnancy, it has been later advised to suture the anterior uterine wall to the peritoneum covering the bladder. While the immediate mortality following this operation was small, the effect upon subsequent pregnancy proved in many cases to be unfortunate. Abortion followed in many instances; in others the uterus was unable to rise in the pelvis, the anterior and posterior walls did not develop symmetrically, and complicated operative treatment became necessary to effect delivery. Several deaths have thus been traced indirectly to the operation of vaginal fixation, and it has not secured for itself a permanent place in surgery. It is seldom performed in America.

The choice between these operations for maintaining the normal forward position of the uterus will depend upon conditions present in different patients and also upon the experience and preference of the operator. Some gynæcologists perform a large number of operations upon the round ligament and seldom suspend the uterus; with others the practice is exactly the reverse. The objection that the round-ligament operation, as suggested by Alexander, does not permit of the inspection and treatment of intra-abdominal disease is obviated, as claimed by certain operators, by the adoption of the radical method. These surgeons virtually perform a cœliotomy upon each side of the abdomen, lay open the entire inguinal canal, open the peritoneum at the internal ring, and, after performing any necessary intra-abdominal operation, they shorten the round ligament and restore the inguinal canal in a manner allied to that adopted for the radical cure of inguinal hernia. This radical method, however, should not be considered in discussing the relative merits of uterine suspension as compared with an external round-ligament operation. The latter gives excellent results when performed by a surgeon who has had abundant experience with it, and is especially adapted to those cases in which the uterus is small and not diseased, in which the element of descent is not important, in which pregnancy is likely to follow later, and in which there are no complicating disorders of the tubes and ovaries. Suspension of the uterus on the other hand may be chosen in those cases in which it is desirable to open the abdomen for other reasons, such as the removal of an irritable but not greatly diseased appendix vermiformis, the separation of peritoneal adhesions, resection of diseased tubes and ovaries, or the removal of the same. While the band of attachment is drawn out into a thin cord and a certain amount of mobility of the uterus is ultimately secured, and while pregnancy in many cases is followed by no complication, the operation is best adapted to those patients who are not liable to become pregnant.

The intra-abdominal operation of shortening the round ligaments may be applied in the same class of cases as those for which the extra-abdominal is usually chosen.

Shortening of the Utero-sacral Ligaments.—This has been done as a direct procedure by several operators who reach the ligaments either through an incision in the posterior vaginal cul-de-sac or from above after opening the abdomen. The object is to draw the cervix backward and somewhat upward, thereby restoring the tendency of the uterus to incline forward as in the normal pelvis, since it is in this position that the uterus best resists the influences which tend to displace it.

Bishop describes (*Lancet*, March 14th, 1903) an operation which aims to reproduce utero-sacral ligaments for the cure of prolapse of the uterus. The abdomen is opened and, with the patient in the Trendelenburg posture, the uterus is drawn up and by a vaginal instrument the posterior vaginal fornix is thrust upward. A stout suture on either side is introduced well into this prominent vaginal tissue from within the abdomen and then attached firmly and deeply to the sacrum, a point being chosen, on either side of the rectum, which is free from vessels and nerves.

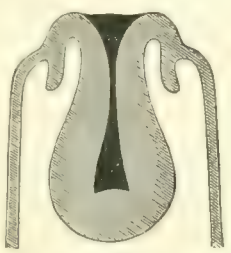

FIG. 4907. Complete inversion of Uterus. (Thomas.) A cupshaped depression is in the place of the uterus. The sound is arrested at the angle of flexion.

Hernia of the Uterus.—The true hernia through the pelvic outlet has been described, but among the curiosities of medicine appear a few cases in which the uterine body has formed a part of the contents of a hernial sac in other regions of the body. Gould and Pyle in their work on "Anomalies and Curiosities of Medicine" quote nineteen cases of hernia of the uterus (C. Debierre: "Les Vices de Conformation des Organes Génitaux et Urinaires de la Femme," Paris, 1892). Thirteen of these cases occurred in inguinal, two in femoral, one in obturator, and three in umbilical hernia.

Manning Simons (*Amer. Jour. of Obst.*, January, 1903, p. 70) describes a case in which both ovaries, both tubes, the bladder and rectum were in a sac formed by the prolapsed vagina, whose anterior and posterior walls had adhered below the cervix uteri. The whole mass protruded from the pelvic outlet.

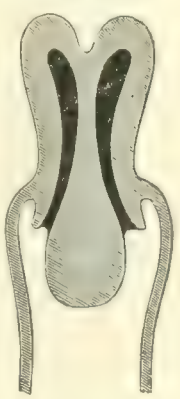

FIG. 4908.—Partial Inversion with Uterine Polypus. (Thomas.)

INVERSION OF THE UTERUS.—The uterine body may be turned inside out or inverted in two principal ways: First, immediately following labor, and as a result of pressure from above, or through traction on the placenta and membranes from below, the fundus of the uterus may become indented (Fig. 4906) and irregular contractions may result in a complete inversion of the organ, so that the endometrium appears in the vagina and the uterus presents itself in that passage as a pear-shaped body (Fig. 4907). As the second cause may be mentioned the contractions produced

by an intra uterine tumor, especially a fibroid tumor, which is attached by a pedicle somewhere in the upper portion of the uterine canal, and whose body is within the grasp of the uterine muscle. Long-continued contractions of the uterus in the effort to expel the tumor may drag down the uterine wall where the pedicle is attached, first producing an indentation (Fig. 4908) and finally, as the tumor is extruded, complete inversion of the organ. This process may require several months, while the accident following labor occurs in a very few minutes.

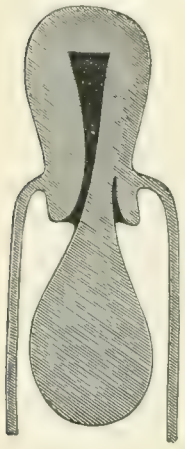

Fig. 4909. Uterine Polypus. (Thomas.) The uterus is in its normal position. The sound passes into its cavity.

Symptoms.—The chief symptom is hemorrhage, which is persistent and often excessive in both varieties. Dragging, bearing down, irritability of the bladder and rectum, and a sense of fulness may be complained of in the chronic variety, while pain and collapse often accompany the hemorrhage of acute inversion.

Diagnosis.—In acute cases little difficulty will be found in recognizing a depression at the former site of the uterine body in the abdomen, and in the vagina a smooth regular tumor with a freely bleeding surface. In some complete cases it will be found that the uterine cervix and the cervical canal have entirely disappeared. In chronic cases in which the inversion is incomplete, a sound entering the cervical canal will serve to define the limits of the protruding body and its relation to the remainder of the uterine structure as felt above the pubis. When a polyp is present without inversion (Fig. 4909) it will be possible to demonstrate the fundus in its normal position. Obscurity is occasionally increased by inflammatory adhesions of the thick stem of a uterine polypoid tumor to the inner surfaces of the uterine canal (Fig. 4910).

Prognosis.—Reduction of the inversion is very seldom spontaneously accomplished. In recent cases the prognosis is good under well-directed efforts at replacement, although in chronic cases very great difficulty may be encountered.

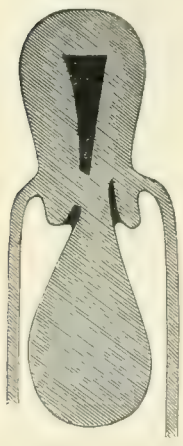

Fig. 4910. Uterine Polypus. Adhesions around neck of polypus obliterate cervical canal.

Treatment.—In acute cases, under anæsthesia, efforts are made to dilate with the thumbs of the operator the contracted cervical ring, while at the same time the presenting fundus is indented and an effort is made to press it through the ring, one portion at a time. A variety of instruments have been devised, in the hope that by means of them the inverted organ may be restored to its normal relations. The end, which is cup-shaped, is designed to fit the fundus and to receive pressure transmitted through a stem which rests against the operator's body or is held in the hand of an assistant. Manual dexterity, however, combined with patience, will usually succeed in effecting the desired reduction, although the process is frequently a difficult one. In long-standing cases the dilatation of the cervical ring is a matter of much greater difficulty. Some device must be used which will make a slow and constant pressure upon the inverted fundus, after the tumor which produced the condition has been removed. In a few cases the reduction has been effected by opening the abdomen and drawing upon the uterine tubes and the upper portion of the fundus, while at the same time pressure was made from below. In this way more ready access is obtained to the contracted cervical ring for the purpose of dilatation; but reduction can usually be accomplished after repeated efforts without opening the peritoneal cavity. Finally, in some cases the wall of the uterus has been split longitudinally from within the vagina, and then, after reduction had been accomplished, the lips of the incision were united by sutures.

George Ervety Shoemaker.

UTERUS, DISEASES OF: MALIGNANT TUMORS.—Definition.—The malignant tumors here referred to, include the various forms of cancer and sarcoma, and deciduoma malignum. The general pathology of the several forms is given elsewhere in this Handbook.

Frequency.—According to the registrar-general of Great Britain in 1900, in England and Wales, 0.975 woman per one thousand of inhabitants died from cancer; and of all female deaths cancer of the uterus caused 1.3 per cent. In 1890 but 0.830 woman per one thousand of inhabitants died from cancer. In New York in 1890 the deaths from cancer in women were 0.37 per thousand of inhabitants, and in 1900 they were 0.43. These figures show the ratio of increase of cancer in women, most of the increase being in cancer of the uterus. It is needless to multiply the statistics.

And of all cases of cancer which occur in the body, William H. Welch found that the uterus was involved in 29.5 per cent. There is no means of accurately determining the ratio between true cancer, sarcoma, and deciduoma malignum.

Sarcoma and deciduoma malignum are very rare. The one fact which is impressively evident is the steady increase in cancer of the uterus. As the disease has been recognized for many years, this increase is real and not "apparent and due to more precise diagnosis."

Age.—In New York in 1890 fifty-seven per cent. of all deaths from cancer were below forty-five years of age. In 1900 fifty-two per cent. were below forty-five years of age. The statement that the disease occurs more frequently than formerly in young women is not correct. The apparent greater frequency is due to the fact that a diagnosis of the disease is now made earlier than it formerly was. The youngest woman having cancer of the uterus in the author's service was twenty-six years of age. The maximum number of cases occur above forty-five years of age. It is exceedingly rare before twenty-five years.

Race.—No race is exempt. It is probable that savage races have it less frequently. The observation used to be made that the negress was exempt. Cullen has proven this not to be the case at the present time. Whether more mulattoes are now found than formerly, and that the pure-blooded negress is less liable, I cannot state.

Causes.—These are actual and contributing. The supposed actual causes of cancer are described elsewhere. The contributing causes are many.

(*a*) *Irritation and Trauma.*—The fact is undoubted that cancer of the cervix is rarely seen in the nulliparous woman, and in a number of instances in which it has occurred in them a trauma, such as dilatation, has preceded its appearance. It appears that nulliparæ have adeno-carcinoma of the body of the uterus about as often as mothers, but that squamous-cell epithelioma is seen most frequently after childbearing or other trauma.

(*b*) *Heredity.*—This is not now believed to be as potent a factor as it was formerly held to be. However, in about twenty per cent. of uterine cancers, another member of the family has had some form of cancer.

(*c*) *Locality.*—In an attempt to find the true cause for cancer all the circumstances under which it occurs have been sought. In these investigations it has been found that certain localities, and even certain houses, have an unusual number of cases. This has given rise to the expression "cancer zones." Those who seek to show the contagiousness of cancer point to these facts as corroborative of their views, but thus far most authori-

ties believe that the unusual prevalence of cancer in certain localities is merely accidental.

Cancer of the Cervix Uteri.—This occurs in two forms: as a squamous-cell epithelioma and as an adeno-carcinoma. Furthermore, either the vaginal part of the cervix or the cervical canal may be involved.

Squamous-cell epithelioma of the cervix is the most frequent form. Squamous epithelium multiplies upon the surface and invades the stroma. Occasionally the epithelial cells are found grouped together so as to form "epithelial pearls." One of the earliest changes in the epithelial cells is the increase in chromatin. The ingrowth of the epithelium precedes the outgrowth, but after a time the epithelium produces delicate filiform projections on the surface of the cervix. The papillary growths consist of branching stroma and epithelium, and are exceedingly vascular. After a time necrosis of the projections takes place and ultimately an ulcer occurs where formerly an outcropping was present.

At first the cervix is nodular and hard, and new vessels may be seen coursing across the nodules. The nodules are of deep color and unequal in size. It is in this state that the disease is seldom recognized. In the state of papillary excrescence the outcroppings appear as delicate papillæ, red in color, bleeding upon the slightest touch, and always pedunculate. They may be so numerous as to form, when massed together, what is appropriately described as a "cauliflower growth." The least touching of such a growth causes bleeding. The excrescence is generally covered by a foul-smelling pus, the result of necrotic changes, and at points minute blood clots may be seen. Without difficulty the finger can be made to penetrate the growth. As ulceration proceeds all traces of the cervix become lost. There is then present at the vaginal vault a cup-shaped ulceration surrounded by raised edges, the surface of the cavity being covered by pus, and the ulcer bleeding easily. The adjoining vaginal wall may be involved, or cancerous foci, the result of secondary "inoculation," may be seen upon the vagina, even at some distance from the cervix.

Extension.—Cancer of the cervix tends to extend bilaterally along the lymphatics in the broad ligament, downward into the vagina, anteriorly toward the bladder, and posteriorly toward the rectum. There is but little tendency for it to grow upward above the internal os, the body of the uterus being usually free even in those who have died from cancer of the cervix.

As the disease extends toward the broad ligaments, the glands lying over the obturator foramina, then those along the iliac arteries, and later the inguinal glands become involved. This glandular involvement is at first due to saprophytic and septic invasion, but later to the presence of cancer elements. It is also true that the epithelia occasionally appear in masses along the veins (Fig. 4911). Cancer of the cervix has little tendency to leave the pelvis. Not only is it at first localized in one part of the uterus, but even to the end it remains as a rule localized in the pelvis. After general pelvic involvement has occurred, all the various phases of pelvic suppuration may be presented: ovarian abscess, pyosalpinx, broad-ligament suppuration, suppurating glands, and peritonitis. The paths along which the cancer extends become ulcerated, and as a result fistulous openings into the bladder, less frequently into the rectum, may be seen. The ureters, for some strange reason, although surrounded by cancer, rarely become corroded.

As the broad ligaments become involved, which involvement takes place, as a rule, more rapidly upon one side, the ureters become obstructed and hydro-ureter results. The rectum may be pressed upon and constipation result. When the rectum or bladder is invaded, the lesions of inflammation of these viscera may be present. The cervical growth may be so large as to block the cervical canal, causing retention of the uterine discharges and pyometra.

Symptoms.—The writer believes that he has discovered a first early symptom of cancer of the cervix which has been furnished by all his patients who were intelligent and cleanly enough to observe such a symptom. Inasmuch as epithelioma of the cervix is characterized by a multiplication of epithelial elements and by increased vascular supply to the cervix, the earliest functional evidence of the disease *is a marked increase in the woman's habitual leucorrhœa, or the occurrence of a whitish leucorrhœa in those who have not previously had it.* In drawing out this symptom, the questioner should first determine the exact amount of discharge which is normal and usual to the individual. In refined women the toilet embraces a certain amount of and frequency in douching, every day or every few days. Without assignable cause such a woman will notice that her habitual leucorrhœa has become markedly increased, and that more frequent douches are needed to keep her tidy. In the case of an old woman whose glandular structures have

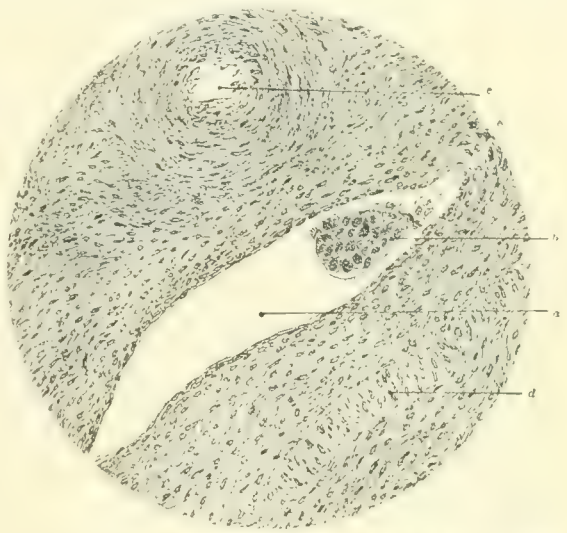

Fig. 4911. Shows a Carcinomatous Mass in a Vein at some Distance from the Original Seat of the Disease. *a*, A vein containing a carcinomatous mass; *b*, isolated mass of carcinomatous tissue; *c*, transverse section of an artery; *d*, section through a vessel; *e*, muscular tissue. (Abel.)

shrunken with the menopause, a return of her forgotten leucorrhœa will be observed. Old women are apt to look upon this as an evidence of rejuvenation, a pathetically mistaken interpretation. The writer has given such prominence to this symptom in order that the attention of readers may be fixed upon it, and that more extended observations by other physicians may either corroborate or correct him. In his cases this symptom has preceded all others by from three to six months, months most valuable to the surgeon and to the woman. But as a rule women, accustomed as they are to vaginal discharges, seldom pay attention to an increase in leucorrhœa. The next symptom is a *change in the type* of the vaginal discharge. From being mucous and odorless, it now becomes watery and often has a putrid odor; or there may be an occasional muddy stain due to the admixture of blood. The menstruations are not altered in periodicity or in character. The presence of a putrid odor is always an indication of molecular death of tissue. Upon coitus, douching, straining, and lifting weights, or even after ordinary exercise, this muddy spotting of the underclothing may be noticed. The putrescence of the discharges and the intermenstrual bleedings become so marked that the attention of even the most indifferent woman is attracted to them. Up to this time the general health of the patient has not suffered. As the broad-ligament lymphatics become infiltrated, there is produced some pain, particularly if the obturator glands enlarge and press upon the obturator nerve. The pain is usually referred to a sacro-iliac joint or to the hip. Should the bladder be invaded, symptoms of cystitis supervene. As the pelvis

becomes generally involved, the symptoms of peritonitis appear. It is remarkable how extensive the uterine degeneration may be without pain being produced. About the time the putrescence of the discharges becomes marked most patients become anæmic or "cachectic." They are usually in good flesh, but the tissues assume a waxen hue The patient is easily fatigued and avoids physical activity. After a time the pelvic pain becomes so great that she lies down a great deal. The consciousness of emitting a disagreeable odor makes of her a recluse. The anæmia is progressive; the severe pains necessitate the use of opiates, and these induce intestinal disturbances; possibly rectal or vesical symptoms supervene, and the physical prostration becomes extreme. In about two years after the onset of the disease the patient dies, either from sheer exhaustion or from some complication.

Physical Signs.—In the stage of infiltration the cervix is nodular, the nodules being of irregular size, deeply colored and evidently vascular. They feel hard, but upon thrusting a probe against them, or seizing them with a bullet forceps, it is seen that they readily break down, exposing bleeding and granular-looking surfaces. The appearance of a nodular and large cervix in a woman past the menopause is significant of cancer, for at that age the cervix should be shrunken. If papillary projections are present, they will be found pedunculate and bleeding upon the slightest touch. They can be scraped off by the nail. The cervical tissue underlying them has the same friability as in the first stage. If the disease has progressed to the formation of a cauliflower growth, this presents itself as a granular outcropping from the cervix, exceedingly friable and bleeding easily. It is always pedunculate and lobulated. After the papillomatous projections have necrosed, there is left an excavated, foul ulcer. The cervix can no longer be detected as a separate structure, but in its place, at the vaginal vault, will be seen the ulcerated excavation; or in its place, particularly in elderly women, the production of connective tissue may predominate, and the place of the cervix be taken up by a puckered, scar-like tissue, "scirrhous cancer." This latter is a very rare condition.

Pain.—As stated, some patients have little pain, but in the later stages of the disease pain of some sort is usual. It may be limited to the pelvis or may radiate to the distribution of the obturator or sciatic nerves

Strength.—Little outward sign of cancer is present until the new growth begins to break down. Then the patient loses flesh, owing to the excessive elimination of nitrogenous material. The muscles fade first, and the fat more slowly. The cachexia is due to absorption of poisonous toxins from the cancer, and to the progressive loss of appetite. Slight leucocytosis is present and the percentage of hæmoglobin lowered.

Pulse and Temperature.—As the patient weakens, the pulse quickens upon the least exertion. In the latter stages of the disease there are irregular rises of temperature

Diagnosis.—In the earliest stage this is to be made from the nodular condition of the cervix, due to cystic degeneration and stellate lacerations; in the papillomatous stage, from condylomata, sloughing polypi, exaggerated conditions of "erosion," and hypertrophy of the cervical glands; and in the stage of ulceration, from tuberculous and chancroidal ulcers, or those due to pressure. Cancerous nodules are exceedingly friable; and if a bullet forceps is hooked into one, it tears its way through upon the exhibition of even a slight traction. The same thing will occur with cystic degeneration of the cervix if much force be used; but when the cystic cervix tears, the gelatinous contents of the cysts are evacuated, whereas a bleeding granular surface is left if the nodule be cancerous. It is interesting to note that cystic degeneration to a marked degree and cancer rarely coexist. The elevations produced by stellate lacerations of the cervix are firm, and have the same consistence as the rest of the cervix

Upon superficial examination, "erosions" of the cervix (cervical folliculitis), particularly if this part of the uterus be torn and everted, resemble cancer in the first of the papillary stage. The surface of the "erosion" is raised, as is that of the cancer; but in cancer each papilla exists as a separate structure, always pedunculate, bleeding upon the least touch, and easily scraped off with the finger nail. None of these features of cancer is present in erosion. Furthermore, beneath carcinomatous papillæ the infiltrated cervix is brittle, while the stroma beneath an "erosion" is increased and the tissues are more firm than normally. Parenthetically, a criticism of the term "erosion" may be uttered. It is an absolute misnomer, for not only is there no erosion or loss of substance, but, on the contrary, there is hypertrophy of the glands. Condylomata of the cervix are firm, covered by epithelium, and, unless ulcerated, do not readily bleed. Sloughing polypi present themselves as single pedunculate growths, exceedingly soft, and as a rule very much larger than the single papillary excrescences of cancer. They often present ulcerated surfaces, but are usually covered by a firm epithelium, giving them a glistening appearance, entirely unlike cancer. Polypi arise from the lining membrane of the cervix, and the cervical stroma is not involved.

Syphilis of the cervix is exceedingly rare, as is chancroid. In a suspected case of syphilis, antisyphilitic treatment gives prompt results, and chancroid is usually accompanied by similar ulcers in other parts of the genitals. In all doubtful cases a portion of the suspected tissue should be excised and submitted to a competent pathologist. Tuberculosis of the cervix is usually secondary to tuberculosis of the vagina or of the body of the uterus.

Old scirrhous cancer of the cervix strongly simulates the cicatrization found about lacerated cervices, but here again the tenaculum shows the disintegration of the cancerous cervix.

In removing tissue for examination, as much of the cervix should be amputated as possible; in any event, the pathologist should be furnished with a section which includes all the elements of the cervix, basement membrane as well as glands.

Treatment.—If the uterus be movable and the disease limited to the cervix, the uterus, ovaries, tubes, and parametric tissue should be removed, either by way of the vagina or by way of the abdomen. In some cases there are distinct contraindications to a radical operation. In such the high amputation of Sims, accompanied by the use of the galvano-cautery, may effect a cure. No internal medication is of avail, except the continuous ingestion of thyroid extract. This, taken in doses of five grains, t.i.d., p.c., not only tends to hold the disease in abeyance for months, but also may cause it to disappear *for a time.*

Adeno-Carcinoma.—The cylindrical epithelium of the cervical canal often extends downward upon the face of the cervix, and this form of cancer may appear upon any portion of the cervix having cylindrical epithelium; but as a rule it occurs within the external os. The disease begins as a submucous, nodular accumulation of cellular elements, proceeds to the production of papillæ, and ulcerates. Or the ulceration may begin before papillæ make their appearance. Not only are the epithelial cells enormously multiplied, but there is also great increase in the glands of the cervix. The papillary excrescences may block the cervix and produce pyometra, but ulceration usually begins before this occurs. The entire supravaginal cervix may be riddled with sinuses, and yet the os externum appear normal. Sloughing and necrosis begin early, and altogether the progress of adeno-carcinoma is more rapid than that of squamous-cell epithelioma. Peritonitis and adnexal lesions also occur more frequently, owing to blocking of the cervical canal, followed by septic endometritis; and cancerous involvement of the bladder occurs more frequently and earlier. The disease is more frequent before the menopause.

Symptoms.—As a rule the first symptom is an increase in the woman's habitual leucorrhœa and in the amount of cervical mucus secreted. As in the case of squamous-cell epithelioma, the indifference of women to any discharge from the vagina causes them to pay no attention

to this important first symptom. Therefore the usual symptom which brings these patients to us is an offensive discharge. Blood-staining of the clothing, occurring between menses, is not seen so early as in squamous-cell epithelioma, because the involved field is within the cervical canal and protected against trauma. Therefore patients with adeno-carcinoma first present themselves with the disease far advanced. The menses are unaffected by the cancer. Women with cancer of the cervix, particularly this type, have been most prolific. The disease is rare in the nulliparous. Pain is not present until the disease has extended outside the uterus.

Upon examining a patient with adeno-carcinoma of the cervix the disease may be seen upon the surface. If it is not visible upon the surface, the introduction of the sound produces sharp bleeding. In fact, so dense is the normal cervical mucosa that it will tolerate a marked degree of trauma without hemorrhage.

Diagnosis.—Tuberculosis of the cervical canal presents all the local signs of adeno-carcinoma. As a primary affection it is exceedingly rare, but must be borne in mind as a possibility. Sloughing polypi present themselves in the form of ulcerated projections, while adeno-carcinoma appears as an excavation when active ulceration is in progress. Small submucous myomata projecting into the cervix may be felt with the finger as hard nodules, not at all resembling cancer. The cervix treats polypi and fibroids projecting into its cavity as foreign bodies, and as a rule it becomes widely gaping.

When the diagnosis is difficult a portion of the cervix may be scraped or cut away and submitted to a pathologist.

Treatment.—If the disease has not extended outside the uterus and there are no contraindications to a radical operation, abdominal ablation of the uterus and adnexa is indicated. Cases are rarely met with early enough to admit of the vaginal operation being successfully performed.

Cancer of the Uterine Body.—This occurs in from six to ten per cent. of all cases of cancer. It is the form of cancer which nulliparous women usually have. The type is nearly always the adeno-carcinomatous. The disease begins at one point in the endometrium, and from there tends to spread. The lesions are similar to those in the cervix—slender papillary outgrowths from the surface of the endometrium, underlying which is a spot of infiltration. The papillæ may entirely fill the uterus and cause marked enlargement of the organ. The uterus becomes soft and boggy. As the cancer grows and sloughs a septic endometritis occurs, and pelvic lymphangitis and salpingitis are common sequelæ.

Symptoms.—About three-fourths of the women are past the menopause. The first symptom is sometimes bleeding, sometimes a watery discharge. This may appear as a spotting of the clothing, or a rather sharp hemorrhage may occur. If the patient is menstruating, the menses are increased, and shortly she has intermenstrual leaking of blood. The uterus resents the presence of the growth, and irregular uterine cramps are often observed. Some patients complain of lancinating pains shooting through the uterus. Cancer of the uterine body produces early in its course symptoms which attract the patient's attention; therefore the cases are seen early. Furthermore, it is of slower progress than cancer of the cervix; and, as the corpus uteri is free from attachments to other organs, extension outward does not occur so soon as in cancer of the cervix. Cancer of the uterine body extends through the lymphatics and not by progressively invading the tubes and ovaries. About half of the women are sterile.

Diagnosis.—Sloughing uterine polypi, sloughing submucous fibromyoma (particularly if cystic), hypertrophic endometritis, retained bits of placenta, tubal pregnancy, uterine sarcoma, tuberculosis of the endometrium, all produce symptoms similar to those arising from corporeal cancer. I shall not attempt a detailed statement of each of these diseases for the purpose of drawing fine distinctions in the gradations of the symptoms. The sole positive test is the microscopic examination of the scrapings secured by a curette.

Treatment.—Unless too firmly fixed in the pelvis by glandular involvement, the uterus should be removed by way of the vagina. Recurrence after three years takes place in only about thirty per cent. of the cases. If all the operations could be done in the first few months, recurrence would be rare. In cases too far progressed to admit of a radical operation, the uterus should be curetted and cauterized by the galvano-cautery.

The Operative Treatment of Carcinoma of the Uterus.—This is of two very distinct and markedly differing kinds: those procedures which may be called radical, and those which are solely palliative.

Indications for the Various Radical Operations for Cancer of the Uterus.—*Cancer of the Cervix Uteri.*—As a general proposition it may be stated that whenever malignant disease of the cervix is discovered and is limited to the uterine tissue a radical operation is indicated. In certain cases the general condition of the patient may be so poor that to subject her to a grave operation would be fraught with too great danger. Advanced lung disease, nephritis, and mitral disease, as a rule, contraindicate ablation of the cancerous uterus. As a converse proposition, it may be laid down that whenever the cancer has extended beyond the uterine tissue, radical work is out of the question. Such extension reveals itself in a greater or less density in the pericervical tissues, fixity of the cervix, and, remotely, glandular enlargements. But these conditions are also brought about by inflammatory lesions, and these latter must be eliminated as causes for the fixity of the cervix before the propriety of a radical operation can be determined. There is a surgical rule, with its corollary, that all operations for cancer shall proceed through normal tissues, and that no radical operation shall be attempted unless the section of the tissues can pass outside the cancerous field; for the scope of any proposed operation is determined not so much by the fact that this or that fraction of tissue is involved in the cancerous invasion as by the tendency of cancer to recur after removal. And the merits of any operation for the relief of this condition are determined by the ultimate results rather than by the immediate. Good ultimate results are not to be expected when the cancer has extended beyond the uterus. And, furthermore, the less the involvement of the uterus itself, the better the remote results following operation. Therefore cancer which is diagnosticated only by the microscope is less likely to recur than that which is revealed by the symptoms which it produces. So, then, the earlier cancer is diagnosticated the clearer the indications for radical operation and the better the results from such operation, both immediate and remote. Even when bimanual examination demonstrates that the uterus is perfectly movable, cystoscopic examination will often show that the cervico-vesical wall is involved. This involvement will cause rounded elevations beneath the vesical mucosa.

The great problem which confronts the surgeon is the determination of the distance, from the cancer field, to which his section of the tissues must proceed. It may be stated that in epithelioma the tissues may be severed closer to the involved field than in adeno-carcinoma. Whether this clinical observation is due to the lesser virulence and slower progress of epithelioma, or to the fact that as a rule epithelioma is usually, because of the nature of its growth, discovered sooner than adeno-carcinoma, I do not know. But it is my belief that epithelioma of the cervix is far less malignant than adeno-carcinoma. However, the rule in operating is to keep as far away from the cervix as possible. There are two routes for operating upon cancer of the cervix: the vaginal and the abdominal. And of all cases of cancer of the uterus which come to us for treatment, scarcely ten per cent. can be subjected to any radical operation.

(a) Indications for the Radical Vaginal Operation.—These are to be found in the immediate mortality and in the ultimate results.

The death rate from vaginal hysterectomy in cancer of the cervix should not be more than five per cent. It is

most difficult to determine precisely the ultimate results because so many patients are lost sight of, and the groups of cases falling into the hands of different operators vary so much in the extent of the involvement. Of all cases operated upon by the vaginal route, about sixty per cent. recur within the first year after operation. Of the remainder, not more than twenty per cent. are free from recurrence after five years. And these results are found by those who are thorough masters of technique.

Fig. 4912.—The Forceps Operation for the Removal of a Cancerous Mass through the Vagina. The forceps are shown grasping the bases of the broad ligaments. All the tissues have been cut so as to free the cervix upon all sides. (Pryor.)

Vaginal hysterectomy for cancer of the cervix is an operation which can be rapidly performed and does not necessitate a profound degree of narcosis. It is therefore indicated in those who are aged and who would not for other reasons stand a more severe and prolonged operation. If it is indicated at all, it is in old women, in very stout women, and in those with nephritis or cardiac disease who are suffering from epithelioma. It is the author's belief that a less severe operation gives results equally good remotely and far better immediately. I refer to the high amputation of Dr. John Byrne. And when we reflect that the radical vaginal operation is limited to cervical cancers which have not extended beyond the uterus, while the procedure of Byrne is applicable, and always with benefit, to all cases in which the disease has not actually invaded the bladder or bowel, we can see the greater value of Byrne's operation.

The Operation.—The patient is placed on the back in the lithotomy posture. All necrotic and cancerous tissue about the cervix should be scraped and cut away. The cervix is then closed by a series of heavy silk sutures. These effectually prevent soiling the wound by cancer elements and furnish excellent traction strings. The uterus must be removed *en masse*, and without hemisection and morcellation. The cervix is now entirely circled either by the scissors or by a cautery knife, preferably the latter. The line of incision must be as far away from the cervix as possible; posteriorly at the lowest limit of the pouch of Douglas, laterally near the ureteral lines, and anteriorly at that point beneath the bladder which will just escape entering that viscus. Approximately this cuff of cervical tissue will not be over one-fourth of an inch in depth. The posterior, anterior, and lateral vaginal walls are retracted by assistants, one of whom pulls the cervix down. The operator now carefully dissects up the vaginal cuff by means of toothed forceps and scissors. He next enters the posterior cul-de-sac and extends the lateral margins of this incision by his fingers until the bases of the broad ligaments are reached. Into this posterior opening a gauze pad is introduced to catch fluids and prevent prolapse of the intestines. The operator then turns his attention to separating the bladder from the uterus. This must be accomplished slowly by means of the toothed forceps and scissors; more rapidly by using the index finger to peel up the vesical tissues.

When the vesico-uterine fold of peritoneum has been severed, the lateral borders of the anterior incision are extended by means of the fingers. The uterus now hangs by its lateral supports only. It is important to release the ureters from their associations with the loose tissue about the cervix. This is accomplished by gently shoving the tissues away from the cervix first on one side, then on the other, anteriorly and posteriorly. It may be doubted whether the ureters can be laterally displaced in this manner. I have many times demonstrated it upon the cadaver. This separation of cervix from ureters is still further increased by drawing down the uterus and lifting the bladder with the trowel. While this is being done one index finger is introduced behind the uterus, and the tissues upon one side, then upon the other, are grasped by forceps. The bases of the broad ligaments upon each side are in this manner grasped, together with the uterine arteries. Before the forceps are locked they should be slowly worked outward as close to the ureters as possible and without wounding them. After locking the forceps the tissues are cut close to them up to the points of the forceps (Fig. 4912). These two forceps must also embrace the insertions of the utero-sacral ligaments. The uterus now hangs by the tops of the broad ligaments and by the round ligaments. In order that these may be secured without risk of wounding the gut, the cervix is released and the body of the uterus delivered beneath the bladder (Fig. 4913). The ovaries are drawn out also and held by suitable forceps. A forceps is then applied from above downward upon the right side outside the ovary, with its points lapping the forceps below and internal to it (Fig. 4914). The broad ligament and round ligament are cut and the uterus swings out of the pelvis. It is an easy matter now to grasp the ovarian artery on the left side and remove the uterus (Fig. 4915). If the operator prefers to do so, he may now substitute ligatures of stout tendon for the forceps. These ligatures are passed by the large aneurism needle first to the bases of the broad ligaments and then to the tops. I always ligate the round ligaments separately to guard against their pulling out of the loop of the ligature, thus loosening it and causing secondary hemorrhage. Care must be exercised in removing the forceps lest the stumps slip away from the operator. He should attach a fine artery forceps to the cut end of the artery, and then, as an assistant loosens the large forceps, the operator ties down hard and makes the second knot as rapidly as possible before the elasticity of the stump loosens the first knot. My individual preference is for the use of the forceps exclusively. If this is done, the

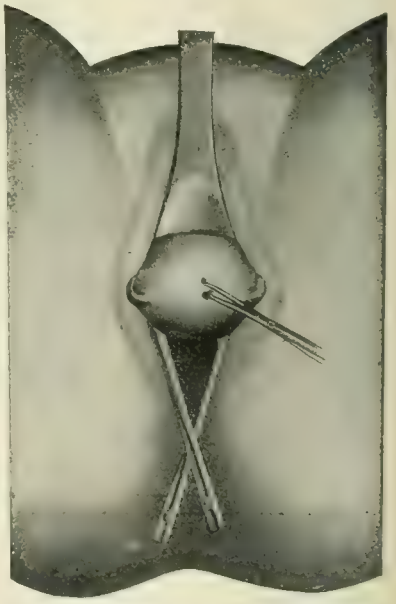

Fig. 4913. The cervix has been pushed up, and the fundus uteri is shown pulled down beneath the bladder. The insertions of the Fallopian tubes into the fundus are shown. (Pryor.)

wound is dressed as in the similar operation for pus. If ligatures are used, these are cut short and the stumps allowed to retract upward. The centre of the wound is then closed by several sutures of tendon, which unite the anterior and posterior cut edges of the vagina.

FIG. 4914.—The retractors have been withdrawn and the right ovary and tube are shown grasped by the thumb in front of the fundus uteri. The forceps is grasping the top of the right broad ligament. (Pryor.)

Intra-abdominal pressure will force the peritoneal edges together. A snug drain of iodoform gauze is inserted upon each side up to the stumps of the uterine arteries so as to prevent prolapse of the intestines or omentum, and the vagina is loosely packed with iodoform gauze. If ligatures are used the stumps do not slough, while forceps, if left on, always cause sloughing. It is because of this effect of forceps that I always use them. With ligatures the stumps remain vitalized, while with forceps they come away. Therefore forceps remove more tissue than the ligatures, and broad removal of tissue is what we desire when operating for cancer. The dressings are removed and renewed at the end of seven days.

(*b*) *Indications for Abdominal Ablation of the Cancerous Uterus.*—Inasmuch as the abdominal operation allows the operator to secure the ovarian vessels at the pelvic brim and the uterine arteries outside the ureters; and, further, as by this operation not only the individual lymph glands, but also the lymph channels in the broad ligaments and the greater part of the vagina, if this should be found necessary, can be removed, I always perform this operation for cancer of the cervix if a radical operation is indicated. The operation permits the broadest section of tissue in an uninvolved field with accurate removal of lymphatics, thus complying with the first surgical requisite. It further admits of this being done under a preliminary hæmostasis, and the vessels and lymphatics are severed before the uterus is subjected to any squeezing, thus eliminating the possibility of extrusion of the cancer elements into the absorbents. Furthermore, complications can be better dealt with by this route. The abdominal route permits the surgeon to remove all those structures to which cancer normally extends and in which it has a tendency to recur. In some quarters there is a tendency to apply the vaginal operation to the early cases, reserving for the abdominal operation those in which there are complications, or in which extension of the cancer outside of the cervix has taken place. If cancer were free from the tendency to recur, such a selection might be proper, but by adopting such tactics the operator is neither just to the operation nor to his patient. If the abdominal operation is the preferable procedure for accomplishing all that surgery can accomplish for this disease when complications already exist, it is, I believe, still more strongly indicated in the early cases. No one has the right to rob a patient suffering from cancer of even a fraction of a per cent. of immunity from recurrence. In all cases it is the surgeon's duty to do the most radical operation possible, provided this complies with the surgical and anatomical requirements of the case and does not carry a prohibitive mortality. A woman with early cancer has a greater right to a radical

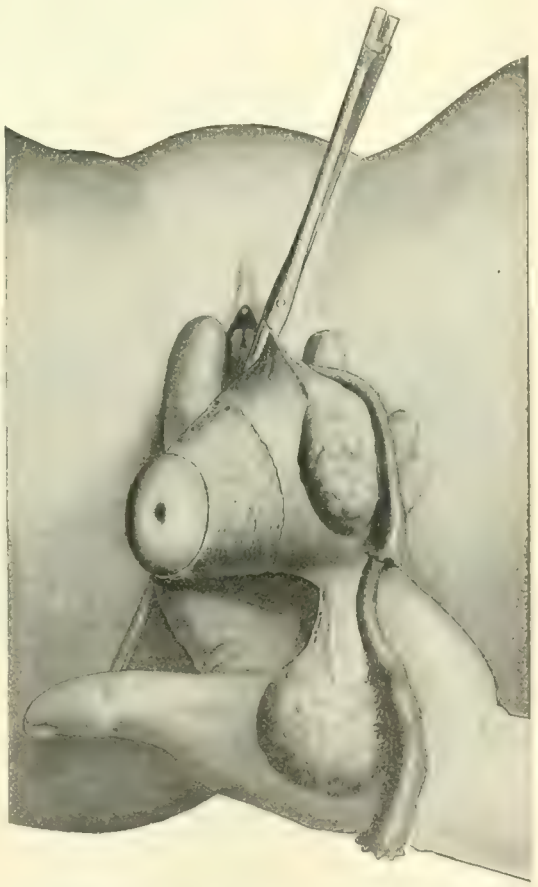

FIG. 4915.—Upon cutting the uterus loose upon the right side, it is made to swing entirely out of the body, so that its posterior surface presents itself, and the forceps is shown grasping the top of the left broad ligament, the last pair of forceps to be applied. (Pryor.)

operation than one with the disease in a later stage, for her chances of recovery and of acquiring immunity against recurrence are greater.

The operation has been before the profession for too short a time justly to estimate the ultimate results. It has been performed by me thirty-four times with three deaths, 8.8 per cent. mortality. In no case in which the

parametrium was not already involved has there been recurrence as early as at the end of one year. The first operation was done five years ago, and the patient is still alive, free from recurrence. In the three fatal cases the causes of death were respectively angina pectoris due to arteriosclerosis, nephritis, and endarteritis obliterans. An extended report will be made at a future date. Enough has been said here to furnish reasons for the procedure.

The Operation. The Vaginal Stage.—The uterus is curetted and all cancerous spots are cut away. The cervix is then thoroughly roasted with the dome-shaped cautery. The vagina is now cleansed, and a self-retaining catheter introduced and left open to drain the bladder. This stage has been conducted by the first assistant, who now resterilizes his hands. The patient is then placed in position for laparotomy.

The Abdominal Stage.—A median incision is made from the pubes to the umbilicus. It is necessary to go through the pyramidalis muscle down to the pubic cartilage. If the woman be fat, the umbilicus is removed and the incision extended above this. Upon entering the abdomen the table is lowered into the exaggerated Trendelenburg position. The intestines and omentum are gently taken from the pelvis and placed in the abdomen, and the sigmoid flexure is straightened out. The curvature of the loins upon each side of the spine above the pelvic brim is carefully and accurately filled with gauze pads, and other pads are used so as to make a complete dam across the body at the upper end of the incision, holding the intestines back. The table is now raised so as to be almost horizontal. A careful survey of the field is made, but rapidly. I then pick up the ovarian vessels of one side at the pelvic brim before they cross the external iliac artery and ligate them. Provisional ligatures are then applied near the ovaries. The same is done on the other side. The broad ligaments between are cut close to the first ligatures, which latter are cut short. The round ligaments are seized by artery forceps, drawn out, ligated close to the internal inguinal rings, and cut short. Beginning upon the right side the peritoneum is split upon a director from the point of the first cut, along the pelvic brim below the internal iliac artery, to the vesico-uterine fold. This having been done on each side and the two cuts united by a third across the bladder at the vesico-uterine fold, the peritoneal covering of the organs to be removed is severed at all points except posteriorly. Using the fingers only, I push (on one side at a time) the lower flap of peritoneum, in which should be the ureter, away from the upper, feeling for the pulsation of the common iliac artery. This blunt dissection proceeds down into the pelvis until the internal iliac is found. At a point over this, about one-half an inch below the bifurcation of the common iliac, the internal iliac is carefully exposed. For this purpose I use toothed forceps and Sims' blunt vesico-vaginal scissors. It will be seen that the artery is accompanied, as a rule, by one vein, which usually lies below it; sometimes it is accompanied by two veins. The aneurism needle is passed unthreaded around the vessel from within out. It should then be threaded with a chromicized tendon one-sixteenth of an inch in diameter, perfectly round and tested. This is drawn around the vessel. The first knot is made with one turn of the strand and tied. It should be tied slowly without lifting the artery, and by a pressure of about two pounds so as to approximate without rupturing the intima walls. The second knot is carefully tied. If pulsation is found below the ligature another is passed and tied. The ligatures are cut short. To one side of the bladder, beneath the horizontal pubic ramus, the loose areolar tissue and fat are spread apart by the fingers so as to expose the white obturator nerve. The needle carrying a fine tendon is passed around the vessels, and they are ligatured. The variations of the obturator artery must be borne in mind at this stage. The dissection described above and the ligations are repeated upon the other side. These eight preliminary ligations have cut off all blood supply through the ovarian, round ligament, uterine, superior vesical, pubic, obturator, gluteal and sciatic arteries, and sometimes through the ilio-lumbar. The field of operation will be bloodless except from severed veins and anastomoses low down in the pelvis. I next dissect out the ureters to the point where they pass beneath the uterine arteries, ligate these arteries at their origins from the internal iliacs as a precaution, and trace the ureters forward well up to their insertion into the bladder. All fat in the obturator foramina about the upper third of the vagina and between the iliac vessels, together with all glands which are visible, are now removed. Particular attention is paid to the bases of the broad ligaments and obturator foramina, to remove all lymphatics and glands. While the ureters are held up, the operator dissects the bladder from the uterus and upper half of the vagina. In freeing the ureters they should be dissected entirely away from the peritoneal flaps, otherwise much fat will be left clinging to them. I usually at this stage ligate, as a precaution, the superior vesical and other anterior branches of the internal iliac close to the main artery. The uterus is now held high up so as to put the vagina and utero-sacral ligaments on the stretch, and the vagina and utero-sacral ligaments, with their peritoneal covering, are circled by the scissors below the upper third of the vagina. Deep down in the pelvis the erectile tissue of the vagina will be found bleeding. This is grasped and ligated. All loose bits

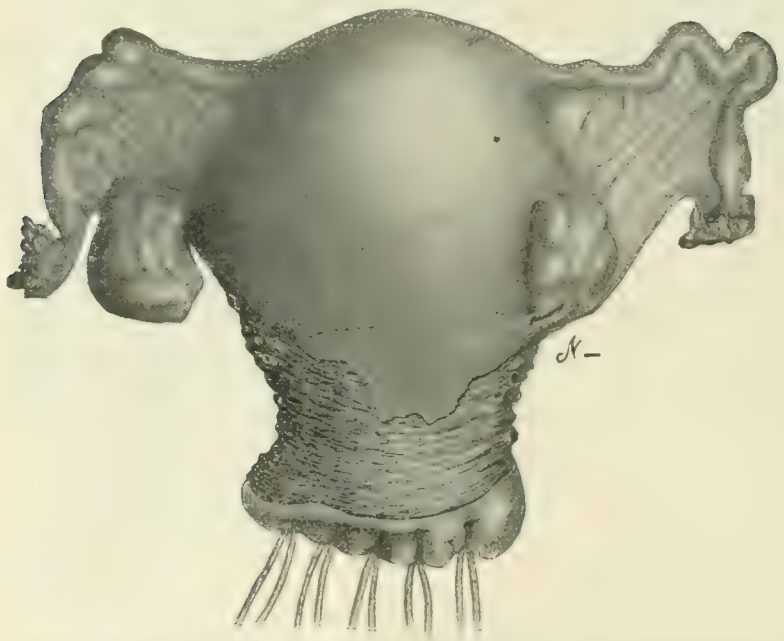

FIG. 4916. A Specimen of a Uterus Removed by Vaginal Hysterectomy (by the forceps operation). The CERVIX, which was the seat of a cancerous growth in an early stage, is shown closed by heavy silk sutures, which were employed to prevent soiling of the field of operation by the contents of the uterus. (Pryor.)

of fat above the bases of the broad ligaments, between the iliac arteries and between the severed utero-sacral ligaments, are picked out. If the venous bleeding is troublesome the patient may be lowered into Trendelenburg's position while the operation is being completed. The vagina is held open by two forceps and several rolls of gauze are introduced, their ends projecting above the vagina. The ureters are returned to their beds and the peritoneal flaps adjusted by interrupted sutures as far as possible. Upon each side a suture should pass through the round ligament, which is stout, and then through the fold of peritoneum at the sides of the rectum. It is unnecessary to suture the rectum to the bladder, as they will fall together (Fig. 4917).

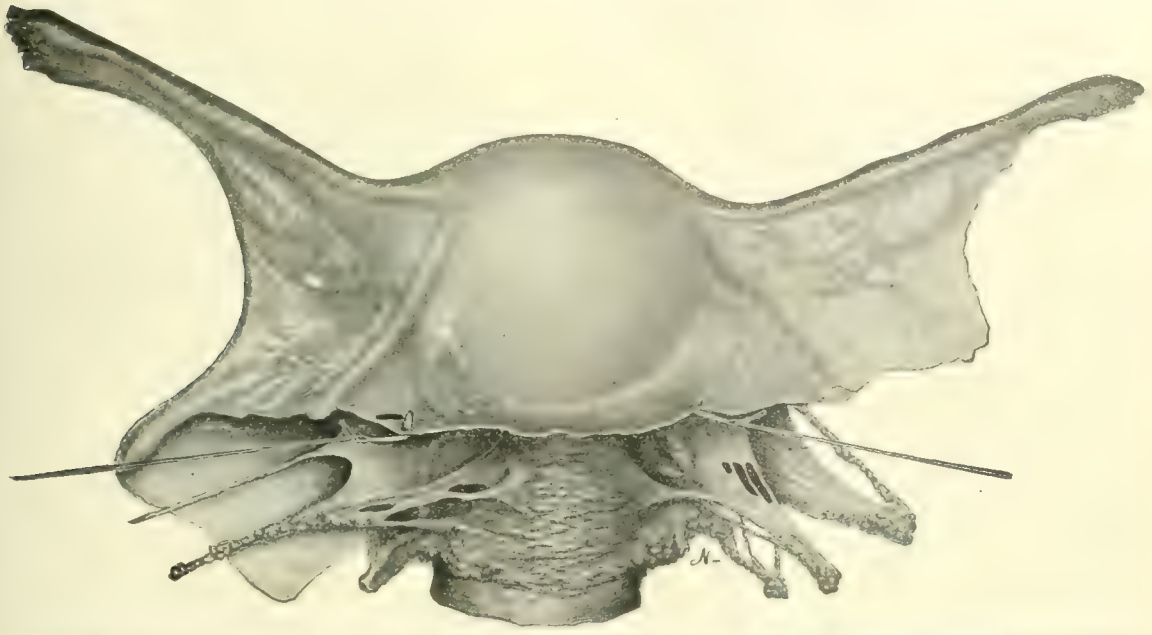

FIG. 4917. A Second Specimen of a Uterus which was Removed, by the Author's Method of Abdominal Ablation with Preventive Hæmostasis, on account of Cancerous Involvement of the Cervix. The vaginal cuff and the lymphatics surrounded by fat are well shown. The drawing is from life, the specimen having been preserved in alcohol. (Pryor.)

The field of operation having been closed out, the retaining pads are removed, the sigmoid flexure and the omentum are brought down, and the abdominal wound is closed. The wound is dressed and the patient placed in the lithotomy position. The vaginal dressings are examined and adjusted. In doing this the livid hue of the vulva and buttocks, due to the ligation of the internal iliacs, will be noticed. The patient is given a high enema of one quart of warm saline solution containing two ounces of whiskey. This is done by dropping the head of the table and not by inserting a long rectal tube. If shock is present it is to be treated as detailed elsewhere. The vaginal dressings are removed and renewed at the end of ten days.

High Amputation.—Indications.—In the author's opinion, the few cases which cannot stand the strain of the perfected abdominal operation will receive a better ultimate result, with less immediate risk, from the operation now about to be discussed than from vaginal hysterectomy. It has been shown that cancer of the cervix has little tendency to ascend above the internal os. It is, therefore, in operating for cancer of the cervix, not necessary to proceed above the internal os. The true indication is for a removal of the upper third of the vagina and the parametric tissue and glands outside the ureter. This is accomplished only by laparotomy, never by vaginal hysterectomy. Vaginal hysterectomy may then be termed an operation of purely local application, such as is amputation of the mamma without muscular and glandular extirpation. It will be seen how thorough a procedure is the high amputation with cauterization.

The Operation.—The patient may be in either the lithotomy or the Sims position. I prefer the former. Wooden retractors are preferable. If metal ones are used they must be frequently cooled by iced water. The uterus is curetted and the cervix amputated by Sims' method. The diverging tenaculum is then introduced into the uterine canal and the excavated stump drawn down. A sharp-pointed knife, curved on the flat, is inserted into the tissues, and a hollow cone of tissue is removed. The tenaculum is again introduced and another cone removed. This is repeated until the uterus is excavated, so that upon digital examination nothing remains of the cervix but a thin shell of tissue. The resulting cavity leads by a broad opening into the uterine cavity, and there should be no constriction at the former site of the internal os. The wound made by the successive applications of the knife should open downward as a cone with a broad base.

The operator now introduces the dome-shaped electrode, cold, as high up as the fundus uteri and turns on the current sufficiently to heat the knife white. It is held in one position until all bleeding stops and the adjacent tissues are charred black. This takes about fifteen minutes. The heat radiates in all directions, and while being applied frequent applications of gauze, wrung out in iced water, are to be made to the vaginal retractors. The staff of the cautery must, of course, not be allowed to touch the retractors. After thus cooking the corpus uteri the current is turned off and the cautery is withdrawn as far down as the cervix. If it is arrested at this point it is because the cervix has not been properly excavated by the knife. The cautery is next held within the cervical excavation and the current turned on. Not only should the heat convert the remains of the cervix into a carbonized mass, but the grayish tint assumed by the adjacent vagina shows that it, too, is destroyed. As the cervical cavity has been thinned out, less time is required to destroy it than in the case of the corpus. In fact, the corpus is so thick that the area of carbonized tissue protects it, and I have never seen it all slough away. The application of the cautery to the cervix

must be most thorough. It is more often done incompletely than in an adequately thorough manner. It is almost needless to say that the heat produces a sterilized wound. It must also undoubtedly destroy the pericervical tissues, particularly the less vitalized cancer cells, throughout quite an area.

The wound is not packed, but when a discharge begins the patient is put on mild antiseptic douches. Surprisingly little pain results. Advanced cases are no bar to the operation. It exerts a retarding effect in all cases of cancer of the cervix uteri. Instead of removing the tissues by knife and then applying the cautery, the entire operation may be performed by the cautery knife, but more slowly.

The Treatment of Advanced Carcinoma of the Cervix Uteri.—This embraces removal of all sloughy and necrotic tissue, so far as is possible, in order to secure local cleanliness. During the application of the curette and scissors frequent digital examinations should be made to determine the thickness of the tissue remaining around the cavity. Should the peritoneal cavity or the rectum or bladder be entered, the patient's danger is much augmented. If the peritoneal cavity is entered it should be drained, not sutured; and if the bladder or rectum be wounded suture is useless, for cancerous tissues will not unite, and consequently the organ entered must be kept empty in the hope, usually vain, that the opening will close. If the peritoneal cavity is entered the drainage is to be effected by means of a catheter; but if the rectum is penetrated a rectal tube should be used for this purpose. In cases in which no damage has been done to any adjacent organ, after all sloughing tissue has been cut and scraped away, the bleeding is to be checked by the application of the galvano-cautery. This cauterization will produce a superficial slough, which in a few days will separate, leaving a granulating wound. Further removal of tissue can be secured by the following method of treatment: Thin circular pieces of cotton, about one half an inch in diameter, are squeezed out in an aqueous solution of chloride of zinc of twenty-per-cent. strength. These are packed snugly all around the cervical cavity so as completely to fill it. Over the whole the vaginal vault is packed with large pieces of cotton wrung out in a saturated solution of bicarbonate of soda. This is essential, because as the serum percolates through the zinc-laden cotton it would cauterize the vagina unless caught and neutralized by the soda solution.

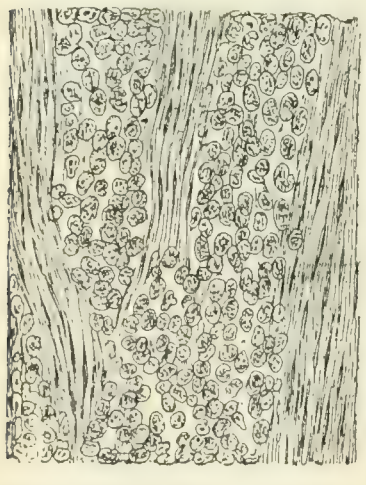

Fig. 4918.—Round-cell Sarcoma of the Uterine Wall, of the usual type. Wyder.)

The dressing is left in for two days. Upon its removal the cervical cavity will be found lined by a grayish slough. Two days later this can be picked away by forceps. In this way repeated sloughs can be produced and removed. When the physician is not provided with an actual cautery, this treatment by means of caustic solutions can be begun after the operation for removal of the cancerous outcroppings, as soon as the bleeding has ceased. I have tried all the various methods of local treatment and find this the simplest and most efficacious. Immediately upon the completion of this treatment the patient should be put on thyroid extract. I have seen good results follow in many cases, and in no case have I failed to see the disease arrested, for a time at least. The thyroid should be pushed to the point of tolerance.

Pain in carcinoma must be relieved by opiates. At first, codeine suppositories are employed, then the stronger preparations of opium.

Section of the spinal nerves I cannot recommend.

Hemorrhages occurring during the course of cancer are best treated by tamponade with vinegar-soaked cotton.

As the pelvis becomes blocked with cancer masses, obstruction of the bowel may occur. It is then the surgeon's duty to perform colostomy.

The rapidity of growth of a cancer of the uterus may be checked by ligating the blood-vessels which nourish it. The plan which I adopt—and which, I believe, I was the first to advocate—is to ligate, through the median abdominal incision, the ovarian, the internal iliac, and the obturator arteries. When the operation is completed, a short incision is made into the peritoneum—one just long enough to enable the operator to reach the vessels. After completion of this operation the cancer masses are scraped away through the vagina, and every facility is offered for the freest escape of the necrosing tissue. The patient is put upon thyroid extract and tonics. By this treatment life is much prolonged and suffering diminished.

Other Methods of Treatment.—Serum therapy has been employed in a number of cases and in various forms, but without benefit. The cases reported to be relieved have upon critical examination proved worthless for statistics.

Owing to the inaccessibility of the cancerous uterus, the *x*-ray treatment can be carried out only with difficulty. It is as yet in a purely experimental stage.

Injections, into the cancer mass, of various drugs, such as methylene blue and alcohol, have been employed, but with little or no benefit.

Sarcoma of the Uterus.—*Frequency.*—Von Franqué, Gualt, Gessner, and Roger Williams, in analyzing 19,263 uterine tumors, found sarcoma but 44 times. In 1894 J. Whitridge Williams, of the Johns Hopkins Hospital, could find in literature reports of but 144 cases, in 34 of which the cervix alone was involved. The disease is undoubtedly more frequent than these reports would indicate, being often classed as fibromyoma in its beginning, and as cancer after ulceration has set in.

Age.—Sarcoma of the uterus is most frequent before the menopause. Gusserow, in analyzing 73 cases, found 52 under fifty years of age. The youngest child in which it has occurred, according to the report of Holländer, was but seven months old.

Fertility.—About forty per cent. of sarcomatous women are sterile, and in those who bear children the average to each is 1.46 children.

Pathology.—The disease may occur as either a spindle-cell or a round-cell sarcoma. It may involve the mucous membranes of the organ or its parenchyma.

Sarcoma of the Cervix. The cellular invasion becomes so great as to produce knobbed projections into the vagina. The growth is hard and nodular at first, but after a time it sloughs. Or there may be "grape-like" polypi hanging from the cervix. These are always multiple, oval in shape, and yellowish-brown in color, and about one-third of an inch in diameter. They are translucent and easily broken, affording escape to a thick fluid. They strongly resemble a portion of a hydatidiform mole. These projections are composed of epithelium overlying layers of sarcoma cells, with clear spaces between.

Sarcoma of the Corpus Uteri. The surface of the uterine cavity is nodular but smooth, but may be rough after ulceration begins.

Symptoms.—The growth causes a general enlargement of the tissues in which it arises. The uterus is increased in size, is movable until the surroundings become involved by an extension of the new growth, is insensitive, and in all respects resembles either fibromyoma or cancer.

But one form of sarcoma is at all clinically easy of recognition, viz., the "grape-like" form of cervical sarcoma. Even the microscopic diagnosis is often most difficult, and yet upon the microscope alone does a positive diagnosis

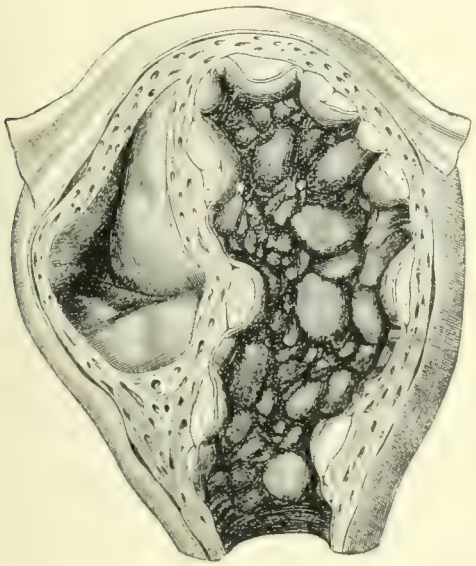

FIG. 4919.—Sarcoma of the Uterine Mucosa, with a Blood Cyst in the Uterine Wall. (Péan.)

rest. The subjective symptoms are at first those of fibromyoma and later of cancer. Sarcoma, however, grows more rapidly than fibromyoma, and the metrorrhagia is in disproportion to the size of the growth. If a nodule projects into the vagina and is seen early, it will be found to present a smoother aspect than cancer and to be more friable than fibroid. The sarcomatous nodules are readily broken into, while submucous fibromyomata, which can be palpated through a dilated cervix, are firm. Sarcoma occurs usually before the menopause, while cancer is most common later in life.

That fibromyoma not uncommonly breaks down into sarcoma must be remembered.

Treatment.—As soon as the diagnosis is made, and if the disease has not progressed too far, abdominal removal of the uterus, ovaries, and tubes is indicated, and should be accomplished by a broad dissection. Although the uterus may be small enough to admit of its removal by the vagina, this should not be attempted because of the exceeding vascularity and friability of these growths. In the removal of the organs by way of the abdomen, the vessels should be ligated at some distance from the uterus so as to add to the prognosis the benefits which such a procedure is known to secure in the treatment of sarcomata.

The injection of Coley's fluid, so successful in the treatment of sarcoma on the surface of the body, is contraindicated in sarcoma of the uterus, owing to the certainty that a fatal sepsis will result.

Even in cases too far advanced for a successful radical operation, the internal iliac, ovarian, and obturator arteries should be ligated.

DECIDUOMA MALIGNUM.—Called also "sarcoma choriocellulare," "syncytioma malignum," "sarcoma deciduocellulare," etc.

Definition.—Deciduoma malignum, first described by Sänger in 1888, is a malignant neoplasm of the uterus occurring only with or after conception.

Frequency.—The disease is about as frequent as sarcoma, 132 cases having been reported up to January, 1902.

Age.—The average age in 124 cases was thirty-two years, but 112 of the 124 cases occurred after the forty-fifth year. The disease is unlike epithelioma in respect of the age at which it occurs.

Fertility.—In 90 of the cases reported the pregnancies are given, and the women averaged 4.2 conceptions. The disease is unlike sarcoma in this regard.

Pathology.—We have not space to discuss the various theories regarding the nature of this interesting disease. The reader is referred to the exhaustive article by Frank Pierce in the *American Journal of Obstetrics* for March, 1902, and also to the article on this subject in the preceding volume of the HANDBOOK. It is my belief that the uteri in which these growths develop are already sarcomatous before the occurrence of the pregnancy which always accompanies deciduoma. The rapidity of the growth after delivery or abortion is not strange, but conforms to the progress of all malignant growths about the pregnant uterus. Microscopically, the growth consists of irregularly shaped protoplasmic masses, of deep color, nucleated, and resembling the syncytium of a chorionic villus; and, in close relation with these, are the cellular masses called Langhans' cells (Fig. 4920).

The growths develop rapidly, the nodular masses soon appearing in all parts of the uterus and pelvis. Metastases are commonly present in fatal cases.

Symptoms.—As already stated, the patient, in every case, either is or has recently been pregnant. About forty per cent. of all cases have been preceded by hydatid mole. Therefore in every case of such a mole, deciduoma malignum should be suspected. The disease is also seen to follow ectopic gestation, normal labor, and abortion. The first symptom after delivery is hemorrhage. This does not occur very soon after delivery, as does a post-partum bleeding, but is first seen during the puerperal months or a little later. The hemorrhages are severe, repeated, and rapidly recurrent. Profound anæmia soon occurs. Soon after the first bleedings a profuse discharge of muddy watery fluid occurs, and is seen when the patient is not bleeding. Metastases occur in the vagina and such distant organs as the lungs, but seldom in the liver.

The patient usually has an elevation of temperature, and an increase in the pulse rate proportionate to the

FIG. 4920.—Syncytioma. *s*, Syncytium; *ns*, necrotic tissue; *l*, leucocytes; *bg*, connective tissue; *c*, cellular (decidual) part of the tumor; *n*, nuclei in the syncytium. (Marchand.)

hemorrhages. Pain is not an early symptom, but occurs when the pelvic nerves become pressed upon by the mass.

Upon examination the enlargement of the uterus is first noted. If the nodules have penetrated the uterine

wall, the peritoneal surface of the uterus will be found nodular. The cervix is commonly dilated enough to admit the examining finger, upon introducing which the friable spongy mass may be felt. It bleeds readily.

Whereas usually the primary tumor is in the uterus, occasionally it will occur first in the vagina.

Deciduoma malignum is of more rapid growth than any other neoplasm.

The patient dies from anæmia, hemorrhage, or metastatic complications.

Diagnosis.—In every case of labor or abortion, in which late hemorrhages occur, an immediate intra-uterine examination is indicated. If a rough surface is found, and if, after the roughnesses have been removed, they soon reappear and are accompanied by hemorrhage, this disease must be suspected and the microscope appealed to. The very frequent association of hydatid mole with deciduoma must compel keen watchfulness in all cases of such moles.

Marchand found that eleven patients died in less than six months, and five within a year, while only one lived as long as three years. When the disease occurs primarily in the vagina, the progress is not so rapid.

Treatment.—As soon as a diagnosis is made, if the disease be limited to the uterus, total abdominal hysterectomy should be performed according to the technique laid down for cancer. *William R. Pryor.*

UTERUS, DISEASES OF: NON-MALIGNANT NEW GROWTHS.—The benign neoplasms affecting the uterus may be divided into two groups according to their histogenesis:

1. Those originating in the uterine parenchyma—fibroma, myoma, and adeno-myoma.

2. Those originating in the remains of embryonal structures—cysts of the Wolffian duct and cysts of the Müllerian duct.

Relative Frequency.—The uterus is extremely prone to invasion by non-malignant neoplasms, especially fibromyomata. Thus, in W. R. Williams' series of 2,649 uterine new growths 883 were myomata. In Gurlt's series of 4,115 uterine neoplasms 481 were fibro-myomata.

The relation of non-malignant new growths of the uterus to malignant ones is 40.62 per cent. of the former to 58.38 per cent. of the latter. The non-malignant glandular tumors occur with much less frequency.

Of the neoplasms originating in the uterine parenchyma the fibromata and myomata are recognized as being of identical structure, varying only in the relative proportion of the fibrous and muscular elements present. They are therefore grouped under the common head of myoma.

Etiology.—The etiology of myomata, in common with other neoplasms, is not as yet understood. These tumors usually develop during the period of sexual maturity, seldom if ever before puberty (never according to Gusserow), and they very rarely appear after the menopause. They are more common in the negro than in the white race, and it would seem from many case-histories that heredity is a predisposing factor.

Myomata may be said to be in general growths of the menstruating uterus, since their greatest activity of growth is during this period. They frequently atrophy after the menopause.

Morphology.—According to their situation uterine myomata are divided into those of the body of the uterus, those of the cervix, and intraligamentous tumors. Those of the body of the uterus are again divided into subserous, interstitial, and submucous tumors.

Strictly speaking, the subserous variety should include only those tumors which are sheathed with peritoneum and lie free in the abdominal cavity, attached to the uterus only by a pedicle. Submucous tumors should include only those which hang free in the uterine cavity, are attached only by a pedicle, and have no muscular coat. All intermediate forms should be designated as interstitial. Ordinarily, however, those growths which project into the abdominal cavity and which originate in the subperitoneal layer of the uterine muscle are called subperitoneal, and those projecting in a like manner into the cavity of the uterus, whether or not they be covered with muscle, are known as submucous tumors.

Besides these situations the tumor may be confined between the layers of the broad ligament, the intraligamentous form.

Subperitoneal myomata are single or multiple nodules which, from being primarily interstitial, have secondarily become subperitoneal. They are closely covered by the peritoneum and are attached to the uterus by a broad pedicle. The tumor is immediateln surrounded by loose connective tissue. Torsion of the pedicle may occur with entire detachment of the tumor from the uterus. Through inflammatory adhesions the growth may become attached to surrounding structures, or it may remain as a migratory tumor in the abdominal cavity. The intraligamentous myoma is a subperitoneal growth arising from the lateral wall of the uterus or from the supravaginal cervix. It pushes apart the peritoneal folds of the broad ligament, and grows either beneath or between them, being thus extraperitoneal. The intraligamentous myoma from its position may exert pressure upon important structures and cause grave symptoms. Usually firmly bound down and in close relation with the pelvic vessels and nerves and the ureters, the intraligamentous myoma is extremely difficult of access.

Interstitial myoma, the primary type of all myomata of the uterus, occurs as circumscribed tumors lying in the uterine wall and attached to the myometrium by a loose connective-tissue capsule. In some cases the capsule cannot be differentiated, and in other rare cases there occurs a diffuse myoma of the myometrium. Submucous myomata are those in which the greater part of the nodule projects into the cavity of the uterus as a polypus, having a pedicle of varying lengths. The tumor is soft in consistence, usually has a free blood supply, and is covered with loose connective tissue and to some extent with endometrium. The pedicle is formed of dense fibromuscular tissue, with a sheath of mucous membrane, and contains a few blood-vessels.

The submucous myomata may become adherent to the neighboring uterine wall by inflammation.

Cervical myomata are of rather infrequent occurrence, forming from five to six per cent. of all uterine myomata. They develop either from the infravaginal or from the supravaginal cervix, the former growing usually into the vagina, the latter into the retrocervical connective tissue.

Myomata in general are multiple; sometimes they are single oval nodules, usually sharply circumscribed and surrounded by a capsule of loose connective tissue. The growth may be hard or soft, is whitish or pinkish in color, and may vary greatly in size. Arising in the myometrium, the tumor develops in the direction of least resistance, and eventually assumes one of the positions described above. On section the tumor is glistening and may be of homogeneous structure, though more frequently it is divided into lobules by septa of dense fibrous tissue which give it, on section, a striated appearance. The consistence of the tumor varies from the soft pure myoma to the hard fibromyoma and the almost stony pure fibroma. The blood-supply of the tumor substance is poor, being limited to a few small vessels. The connective-tissue capsule is freely supplied with large arteries and venous sinuses.

Histologically, myomata are formed of a muscular tissue the cells of which possess the spindle-shaped nuclei and the homogeneous protoplasm characteristic of unstriped muscle in other localities. The muscle bundles are separated into lobules by septa of dense connective tissue. In certain cases this dense connective tissue forms the basis of the tumor. In all cases mast cells of various shapes—long, spindle, ovoid, or round—are present in varying numbers, occurring mostly in the neighborhood of the blood-vessels.

The myometrium undergoes an associated true hypertrophy in interstitial and submucous myomata, as well as in some cases of subperitoneal myomata. The uterine walls become thickened and the cavity is distorted and en-

larged. The endometrium also undergoes hypertrophy in myomata, some cases showing a hyperplasia of the gland substance, some a thickening of the stroma, some both.

In the presence of a large myoma the Fallopian tube frequently is the seat of a salpingitis, while the ovary almost always undergoes a hyperplasia of the connective tissue, with some degeneration in the neighborhood of the blood-vessels.

The myoma itself very frequently undergoes pathological change. Among the conditions which may result are atrophy, calcareous infiltration, fatty degeneration, amyloid degeneration, maceration, myxomatous degeneration, inflammation, necrosis and gangrene, thrombi, telangiectatic change, sarcomatous degeneration, and the association of carcinoma.

Atrophy results when the myoma undergoes a part of the general physiologic involution of the genital system following the puerperium, the menopause, or after a bilateral oöphorectomy. The muscle cells decrease in number and the relative proportion of fibrous matter is greatly increased, the tumor being converted into a dense structure of practically cicatricial tissue. Occasionally the growth entirely disappears.

Calcareous infiltration may take place locally or generally. It occurs with advanced atrophy, and in some instances the entire myoma is converted into a calcareous mass by the deposition of lime salts—the so-called womb stone. Bony changes or osteomyoma have also been described.

Fatty degeneration occurs in the muscle fibres and is frequently found in the interstitial and submucous tumors, rarely in the subperitoneal. It occurs after pregnancy and also in those growths which have a dense consistence.

Amyloid degeneration of the tumor alone or of the tumor and the myometrium may be found, but this change is of rather rare occurrence.

Maceration of the tumor may occur as a result of an acute disturbance of the circulation; the tissue becomes soft, infiltrated with blood, and finally assumes a brownish-green color. Myxomatous degeneration occurs frequently, more especially in the intraligamentous variety, and rarely in the subperitoneal variety. It begins with softening, the consistence of the tumor becomes cystic, and finally cavities filled with mucoid substance are formed in the centre of the nodule. Tumors undergoing myxomatous degeneration increase rapidly in size.

Inflammation, necrosis, and gangrene of myoma are frequent, the pathogenic organisms entering through the vagina, or, in the case of subperitoneal myoma, through the intestines.

Thrombi may be found in the blood-vessels, especially following torsion of the pedicle and incarceration.

Telangiectatic change is an occasional condition. The tumor tissue is infiltrated with numerous dilated blood-vessels. In some instances the lymph vessels may undergo dilatation, as a result of which numerous cystic cavities lined with endothelial cells (cystic myoma) are formed.

Malignant Degeneration.—Myomata may undergo a sarcomatous metaplasia, or they may be associated with carcinoma. The transition into sarcoma is thought to be due to a direct change of the muscle cells into sarcoma cells. The tumors increase rapidly in size, undergo necrotic change, and the sarcoma infiltrates the surrounding structures.

The association of carcinoma with myoma is thought to be due to an inversion of the polypoid growth of the mucous membrane into the myoma tissue, or it is a carcinoma developing from the glandular elements of an adenomyoma, or there may possibly occur a true metaplasia of the myoma elements into carcinoma.

The *symptoms* of myoma uteri are hemorrhage, pain, intermenstrual discharge, and pressure symptoms. Hemorrhage is present in the great majority of myomata of all kinds; it occurs as a menorrhagia or a metrorrhagia. There may be an increase in the menstrual bleeding, or the hemorrhage may appear at irregular intervals, following unwonted exertion, coitus, etc., or it may occur as a continuous bleeding from the uterus. Usually the hemorrhage is not alarming in amount, and can readily be controlled by rest in bed and the exhibition of astringent drugs, as ergot. In some cases, however, a profound and sometimes fatal anæmia is produced. The hemorrhage is independent of the size of the tumor, but varies greatly with its position and variety. Thus the bleeding is most severe in the uterine polyp, less marked in the interstitial variety, and least in the subperitoneal form. Again, the hemorrhage is more severe in the soft and œdematous myomata than in the dense fibrous forms. The hemorrhages are caused by the increased area of the endometrium, due to the uterine enlargement and to a hemorrhagic endometritis set up by the irritating presence of the tumor.

Pain is a more or less constant symptom. It varies greatly in character and degree. It may be referred to the occiput, the top of the head, or the sacral region. Bearing-down and dragging sensations in the pelvis and expulsive contraction of the uterus are frequent. The pain is always increased during the menstrual periods, and during the early growth of the tumor it may be present only at these periods; later, it becomes constant.

Intermenstrual discharge, the result of a profuse secretion from the utricular glands, occurs between the hemorrhages. The secretion is usually thin and serous, and may be very profuse. In some cases in which hemorrhage is not marked its place seems to be occupied by this serous discharge. Dysmenorrhœa is a common symptom.

Pressure may cause many mechanical disturbances: constipation or mucous diarrhœa, hemorrhoids, difficult, painful, and frequent micturition. Pressure upon the ureters may cause hydronephrosis and eventually death from uræmia. Pressure upon the pelvic nerves may cause neuralgia or even paralysis of the legs.

Fatty degeneration and brown atrophy of the heart are sometimes noted. Thrombosis and embolism are frequent complications, especially in the telangiectatic myomata. This is probably the cause of some of the sudden deaths following operations upon these tumors.

The *diagnosis* of myoma is made from a study of the symptoms and a physical examination of the patient. The symptoms described above, while characteristic, are in no sense pathognomonic, and the diagnosis usually depends upon a careful physical examination. In tumors large enough to be palpated through the abdominal wall, the dense consistence and irregular outlines of the myoma may be noted. Bimanual examination detects the general enlargement of the uterus, the outline of the tumor and the consistence, hard and dense, fluctuating or semifluctuating, according as the myoma is hard, œdematous, or cystic. The growth is found to be attached to the uterus and movable with it. Sometimes in the case of a small interstitial myoma a slight elevation or merely an area of induration may be felt. The presence of such an area, together with the increased length of the uterine cavity, is strong evidence of the existence of a small myoma. The symmetrical enlargement of the uterus which occurs in some cases is more difficult of diagnosis.

Differential Diagnosis.—Myomata must be differentiated from pregnancy, ovarian cysts, retroflexion of the uterus, etc. The separation of a myoma from pregnancy is usually easy. The irregular hemorrhage, the mammary changes, the nausea, and the skin pigmentation may be present in both. The absolute signs of pregnancy—the fœtal movements and heart sounds, the bluish discoloration of the ostium vaginæ, and the soft cervix—will usually establish the diagnosis. Should the pregnancy be complicated by myoma the difficulty of diagnosis is much enhanced.

The differentiation between ovarian cysts and myoma is not difficult, and a mistake is not at all serious, cœliotomy being indicated in both conditions.

Small myomata in the posterior uterine wall may be mistaken for retroversion. This mistake may be avoided

by feeling with the abdominal hand the fundus uteri in its normal position and by the passage of a sound.

Treatment.—Operative treatment is usually demanded in a case of myoma. Palliative measures are of little value, and are indicated only where serious degenerative changes in the heart, lungs, or kidneys preclude the possibility of surgical interference. Operation is indicated because of the danger of the accidents possible to myoma, viz., inflammation and infection, malignant degeneration, etc., and because of the very faint hope of spontaneous cure and atrophy of the growth following the menopause. Should the patient be a young woman with a small tumor, and desirous of maternity, the expectant treatment is justifiable. The patient should be warned that the tumor may interfere seriously with labor, may cause her to abort, and may grow with great rapidity during pregnancy. On the other hand, there is a possibility that the tumor may disappear after labor. Should the tumor be intraligamentous and of pelvic growth, expectant treatment is not justifiable, as dangerous pressure symptoms may result and labor be certainly obstructed should pregnancy occur. In the case of a woman who has reached the menopause, in whom menstruation has ceased, and who suffers from no serious symptoms, expectant treatment may be tried in the hope that the disease may become quiescent.

Among palliative measures may be mentioned the exhibition of drugs, electricity, and various palliative operations. Drugs have no effect upon the growth of the tumor. Ergot perhaps does good in arresting hemorrhage in some cases, but is of no other value. Electrolysis has been practised by Martin, Engelmann, Keith, and others, but it does no good; and, on the other hand, it may do positive harm by setting up inflammatory adhesions, thus rendering the subsequent operation more difficult.

Thorough curettage of the uterine cavity, by removing the hemorrhagic and chronically inflamed endometrium, is a very efficient means of checking hemorrhage. The bleeding is usually much diminished for several months after this procedure, though recurrence of the symptom almost invariably occurs. Curettage, which may be expected to check hemorrhage and to remove polypi, is indicated in all those cases in which the physical condition of the patient does not warrant more radical measures.

Ligation of the uterine arteries and broad ligaments to shut off the blood supply of the uterus and thus to cause atrophy of the tumor, has been practised. While this operation seems to have done good in some reported cases, it is now used only as a rare palliative measure. Salpingo-oöphorectomy has been of value in many cases. Its dangers are as great as those of hysterectomy, and at the same time it does not remove the disease. It is not available in all varieties of myomata, and is of no value after the menopause.

Of the radical operations salpingo-oöphoro-hysteromyomectomy is the operation of choice in the great majority of cases. The operation is indicated in the presence of large adherent tumors, when radical measures are necessary, and where degenerative or inflammatory changes are present in the ovaries or Fallopian tubes.

Myomectomy is the least mutilating of the radical operations. Its advantages are the possibility of pregnancy after operation and the avoidance of the surgical menopause. Its dangers are the liability to recurrence of the tumor and the frequency of post-operative hemorrhage. It is also applicable only to isolated pedunculated tumors and some few isolated sessile, interstitial, or broad-ligament growths so situated that they may be easily shelled out without undue injury or loss of tissue. This operation, which preserves the uterus, tubes, and ovaries intact, is the most conservative operation in the treatment of myoma of the uterus.

Further conservative measures are hystero-myomectomy, an operation which leaves the ovaries and tubes intact wherever possible, and a hystero-myomectomy with high amputation of the cervix. This latter procedure is of greatest value in those cases in which total hysterectomy is not necessary and myomectomy is impossible. The tubes and ovaries are left intact, and the uterus is amputated at the highest possible point, so that a portion of the uterine body, lined with corporeal endometrium, even though it be small in amount, may be left in the stump.

Adeno-myomata are rare forms of uterine myomata containing glandular elements. The epithelial structures are derived either from the endometrium or from the remains of the Wolffian body. In those developing from the endometrium the tumors are situated in the anterior, posterior, or lateral uterine wall, and have the usual characteristics of myomata, except for the presence of glandular elements and the absence of capsule. Those derived from the remains of the Wolffian body are found on the posterior surface of a uterine cornu, in the tube, or occasionally in the peripheral layers of the myometrium. These growths occur in the following forms: A dense, hard tumor in which the muscle tissue is in excess of the adenomatous tissue; a cystic tumor with many distinct cystic cavities; a soft adenomyoma in which the adenomatous tissue is in excess and in which germinal epithelium is present; and a telangiectatic adenomyoma.

Histologically, the tumor is composed of muscle tissue containing epithelial canals. The cystic cavities may contain pigment or bloody fluid.

Rhabdomyomata are pedunculated polypi of the cervical canal which always contain sarcomatous elements.

The treatment of adenomyomata should be radical, a supravaginal hysterectomy being the operation practised.

The cysts of the uterus developing from the remains of the Wolffian or Müllerian ducts are of very infrequent occurrence. They are usually small, though they may attain the size of a fœtal head. They are lined with cylindrical or cuboidal epithelium, which may be ciliated. Polypoid pseudoplasms, the outgrowth of subacute inflammatory processes, occur more especially in the cervix, the mucosa of the corpus being rarely affected independently of the cervix. These pseudoplasms are usually small, multiple, soft, vascular growths.

The round ligament, which may properly be considered a part of the uterus, is at times the seat of certain benign neoplasms. Myomata and adenomyomata, having the same histogenesis as similar growths in the uterus, are sometimes observed in this part. Myomata of the round ligament are more common in nulliparæ, and are more frequently found on the right than on the left side. They may be intra- or extraperitoneal, are usually pedunculated, hard, painless and of slow growth, and when they are large they may give rise to pressure symptoms.

Hydrocele of the canal of Nuck may be present, forming a cystic tumor in relation with the round ligament. A true cystic myoma may develop in the parenchyma of the round ligament. Clinically, these tumors are found in the inguinal canal, beneath Poupart's ligament, or in one of the labia majora.

The treatment of these round ligaments consists of extirpation of the sac and direct suture. Should the myomata of the round ligament attain a size sufficient to cause pressure symptoms they should be removed.

Henry D. Beyea.

UTERUS, INVOLUTION, SUBINVOLUTION, AND SUPERINVOLUTION OF THE.—I. Involution.—Involution is the process of retrograde metamorphosis by which the puerperal uterus returns from its condition of physiological hypertrophy to the normal non-gravid state. There is a broader sense in which the word is occasionally used, including those cases of reduction in the size of the uterus following the evacuation of retained contents, as in physometra, hydrometra, or hæmatometra, or after the removal of submucous fibroids, uterine hydatids, or other tumors accompanied by hypertrophy. The processes in these cases are identical, but the latter conditions are relatively so rare that it is fair to disregard them and use the word in its relations to pregnancy only.

Every writer upon the subject calls attention to the wonderful nature of the change which occurs. Striking as is the alteration effected in the uterus during the nine months of gestation, by which its weight is augmented from twenty-one to twenty-four times, even more remarkable, if possible, is the process of involution by reason of its great rapidity. The increase in size of the uterus is due almost wholly to hypertrophy of the individual muscular fibres, together with the development of new fibres from previously existing embryonic cells, this latter process being probably confined to the inner layer of the muscular wall, and occurring wholly during the first six months of pregnancy.

Many authors claim that, in the process of involution of the uterus, the muscle fibres undergo fatty degeneration, that absorption takes place, or that the fatty material is carried off in the lochial discharge, that this process is followed by regeneration, that new cells which develop into muscle fibre are seen in the midst of the fatty mass, and that a new uterus is formed. The blood-vessels, both arteries and veins, participate in the process of fatty degeneration, and from the fragments of the mucous membrane which remain intact at the placental site a new one is formed.

Others of a later date, since histology has developed, claim that it is a process of atrophy—that is, a diminution in volume of the muscle fibres.

Helme [1] has made a study of the process in rabbits at all stages of the process and has examined many specimens immediately after death. He finds no evidence of a fatty degeneration and a later regeneration. There is not a pathological atrophy, but a shrinking of the muscle tissue—a physiological retrogression. It may be a chemical change, but not a fatty change. The contents of the cells become more soluble so that they can pass into the lymph stream. The atrophy continues alike in all parts of the uterus, but there are no groups of degenerated cells found in the midst of the healthy tissue.

At first the muscular fibres which at the end of labor are translucent become cloudy or dusky, and diminish in volume very rapidly for the first thirty-six hours. Then follows a more gradual shrinking up to the tenth day. Helme finds that there is no evidence that old muscle fibres are destroyed and new ones produced, but that it is a retrograde change or shrinking and that the larger fibres simply become smaller. It is simply a diminution in volume.

The change that takes place in the connective tissue is a different process. There is a gradual diminution in amount and a disappearance of the connective tissue. The connective-tissue fibres and cells become granular, and some entirely disappear, while others do not undergo the degeneration.

The veins and arteries of the uterus show the same diminution, and some again entirely disappear.

It would seem that, concerning so universal and carefully observed a phenomenon as involution, there need be no difference of opinion as regards the rate of its progress and the time of its completion, and yet absolute knowledge of the matter does not exist. The modifying conditions are so numerous, and the methods used by which to arrive at conclusions so various, that no two observers appear to agree. Pathologists judge from appearances found after death, clinicians from the relations of the fundus to the symphysis pubis, statisticians from measurements made either with the pelvimeter or with the intra-uterine sound. Sources of error only too readily creep into the observations in each case and seriously affect the deductions. Post-mortem examination furnishes, of course, positive results, and yet who can say how much the retrograde process has been interfered with, in any given case, by the illness causing death, or by the other attending circumstances during life? The relation of the fundus uteri to the pubis may depend more upon the amount of prolapse, version, or flexion, the fulness of bladder and rectum, the size of the pelvic cavity, and the degree of tension of the abdominal walls, than upon the size of the uterus. It has seemed to me that measurement of the vertical diameter of the uterus by means of a pelvimeter must be unreliable, by reason of uncertainty as to the thickness of the abdominal wall, and as to the importance of existing flexion and of longitudinal compression resulting from the necessary expenditure of force.

Unquestionably, the best results must be looked for from the actual measurement of the depth of the uterine cavity in a large number of normal cases, at intervals, during the puerperal month. Much has been done in this line of investigation, and yet I know of no results which are at all satisfactory or conclusive. Up to eight or ten years ago, it was taught that reduction in the size of the uterus was most rapid during the second week after delivery, but that not until the end of six weeks or two months was the normal size regained, and this statement was regarded as authoritative until the appearance of a series of intra-uterine measurements,[2] begun by A. D. Sinclair and continued by W. L. Richardson, both of Boston. From these figures there has frequently been deduced the conclusion that involution is much more rapid than was formerly believed, and teaching has been modified in accordance with this belief. This conclusion has been partially corroborated by Charpentier, though his averages are materially larger than those of Sinclair; and Skene, in his recent work, accepts it completely.

Now were the question at issue merely one of scientific interest, having no important practical bearing upon the management of the puerperal state, it would not properly arise for discussion in this article, but it has a very vital connection with the vexed questions as to how long a patient should keep her bed after delivery, and how much latitude should be permitted her in resuming her customary avocations; and it has also a plain relation to the remaining topics to be considered under this heading. This being the case, it is not out of place here to call in question the accuracy of the reported measurements, and to assert that the old belief, founded upon post-mortem investigation, is the correct one, the one upon which all rules of conduct should be based. The reason for so confident an assertion is the knowledge that the measurements, as reported in the papers above mentioned, vary more with the skill and boldness of the house physician in passing the sound than with the condition of the patient or the duration of her puerperal period. A part of those published were made by myself, and, though septicæmia was rife in the hospital at the time, they evidenced a most phenomenal involution amounting in some cases to superinvolution. These results I knew to be untrustworthy, and yet they corresponded with the work of my predecessors.

I was succeeded in this line of work by Dr. W. J. Otis, who, believing with me that his sound rarely reached the fundus, and fearing to do injury to a soft and friable uterus by the employment of greater force, entered upon the use of a Jennison elastic sound, to which he adapted a sliding marker or guide. With this soft and elastic instrument, used with gentle yet persistent manipulation, the whole aspect of the figures at once changed, and from that time on only once did the measurement fall below three inches. He has very kindly furnished me with the results of his examination in thirty cases, after the adoption of the new instrument, and from his figures I select the following as indicative of the general conclusion. Of the 30 uteri, 6 had a depth of three inches, 5 of three and a half inches, 4 of three and three-quarter inches, and 7 of four inches. The average depth was 3.68 inches, and the average day of measurement was the seventeenth.

I learn from the house physicians of more recent years that the depth of the uterus always increases after a few weeks' experience in measuring, and that the figures are uniformly much greater during the service of some men than they are recorded by others. Though septic influences have been absent of late, yet the average depth, I am assured, is greater rather than less than it was found by Dr. Otis. The fallacy in this method of investigation lies in the fact that the uterus is so softened as to be

easily perforated, or, at least, penetrated by the sound, thus staying the examiner's hand through fear; is often flexed; is not yet lined by normal mucous membrane, but by a soft exudate in which the instrument is readily entangled; and that upon its inner surface is an elevation corresponding to the placental site, an elevation sufficiently great to obstruct the passage of the sound. The custom of examining upon the back tends to increase existing difficulties, so that I believe the fundus is by no means always reached, even by the most skilled observer, and under the most favorable conditions.

A very important series of measurements is reported by Hansen, in the *Zeit. f. Geburt. u. Gyn.*, 1887, a review of which has been made by Parvin.[3] He examined 200 women, making in all 1,048 measurements with the sound. He announces that "the duration of involution was in general ten weeks; the shortest period observed was four weeks, and this in only one case, while the longest period was three months, which was observed in four women." Parvin concludes by stating that "one of the most important practical lessons to be learned from the investigations of Hansen is, that obstetricians should insist upon a longer rest for the puerperal woman. When we remember that many a woman is up and at work two or three weeks after childbirth, and that even those whose circumstances in life do not require labor are frequently participating in social pleasures and fatigues at the end of six weeks or two months, we can easily understand why disorders of the genital organs not infrequently result."

It was also found that involution was delayed in those who did not nurse.

The questions as to the influence upon involution of normal lactation, and of the routine use of ergot after delivery, are eminently practical ones, and deserving of notice. It would seem that so physiological and essential a process as suckling ought to have a favorable influence, especially in view of the intimate relation existing between the breasts and the uterus, any excitation of the former stimulating contractions in the latter. Yet this view is opposed by many observers, notably among the French. Tarnier takes conservative middle ground, holding that "the individual conditions have a much greater influence upon the course of uterine retrogression than lactation." In the face of such contradictory faiths the chances are that Tarnier is correct, and the influence of nursing is a factor of minor importance. My own belief is that it is favorable rather than otherwise, provided, of course, that the patient has sufficient strength and vigor for the physiological performance of the function. Under other circumstances the drain might easily result in such physical deterioration as materially to interfere with the restoration of the uterus.

Unquestionably, it is the custom of the majority of American physicians to administer ergot, as a routine measure, at the close of labor. Subsequently, should the uterus fail to contract firmly or retrogression prove tardy, the exhibition of the drug is continued with anticipation of benefit. Of late years, however, the wisdom of these procedures has been disputed by those who believe, not only that the practice is useless, but that it is actually harmful, it being claimed that involution is retarded thereby. This theory, while given a respectful hearing, has not as yet found favor in practice, the sanction and approval of the profession being still given to the use of ergot as outlined above.

Among other factors in determining the rapidity and completeness of involution are the duration of labor and amount of resultant fatigue; the condition of the patient's health before labor; the occurrence of lacerations of cervix or perineum; the occurrence of septic poisoning, or of local inflammatory conditions from any cause. These matters will receive more especial mention in the consideration of subinvolution. After abortion or miscarriage, unfavorable conditions being absent, involution proceeds as after normal labor, only more slowly.

II. Subinvolution.—Subinvolution is simply a state of persistent incomplete involution, the process having by some means been arrested before the uterus has fully regained its normal state. Corresponding with the intensity of the acting cause and the time of its occurrence, the uterus may remain very large, as at the close of the first week, or it may be only moderately hypertrophied. From this fact probably has arisen much of the uncertainty which still exists as to the exact nature of the condition and of the subsequent changes which take place. So great, in fact, is this uncertainty that few writers can agree even upon a name which suitably indicates the nature of the disease, those who make use of the term "subinvolution" acknowledging that it is only clinical in its application, and by no means covers the progressive pathological changes; those who classify it under the heading "chronic metritis" for the most part disclaiming any belief in its inflammatory origin or course; and the terms "engorgement" and "infarctus" indicating only phases of, or steps in, the progress of the disease. "Chronic parenchymatous metritis" is open to the same objection as "chronic metritis," because suggesting inflammation. Thomas, in absolutely denying any inflammatory element, suggests and uses the title "areolar hyperplasia," as descriptive of a condition of the uterus of which subinvolution is by far the most frequent cause, thus regarding the latter not as a separate disease, but rather as a merely fugitive condition giving rise to "areolar hyperplasia."

However, it matters little what one chooses for a name, if only he recognizes the fact of arrested involution and acts accordingly, as witness the statement of Hart and Barbour[4]: "The term subinvolution is *etiological*, and simply expresses one mode, the most important, in which the condition to be described (chronic metritis) is produced. *Apart from the history*, it is not possible to diagnose between a subinvoluted uterus and one enlarged from chronic metritis alone. Further, the condition of subinvolution is maintained by the process of chronic metritis—that is, by the formation of connective tissue. Finally, the treatment is the same in both cases." In other words, whatever the conditions in the early stages of the disease,—whether involution has been arrested in the first puerperal week by septic absorption, with a resultant uterine or peri-uterine inflammation, or in the fourth week by a mechanical displacement,—there results sooner or later, in consequence of continued hyperæmia and irritation, a proliferation of connective tissue, with ultimate contraction and hardening of the whole uterine mass. These later stages constitute the "chronic metritis," or "areolar hyperplasia," above mentioned.

As regards the method by which the normal enlargement is perpetuated, there are at least two definite and diametrically opposed views, both of which, as has already been intimated, may be consistently held to be correct. Courty says[5]: "The hypertrophy of the uterus, by failure of the retrograde evolution, is a pathological hypertrophy by its permanence, but resulting from a purely physiological hypertrophy in its origin." He quotes West as claiming a fatty change with lack of absorption of the product, and claims the contrary to be true. He states that there is not a change in the texture of the uterus, but a "persistence in the number and volume of its component elements. There is not a fatty change of the uterus," but an hypertrophy by excess of nutrition.

On the other hand, Hart and Barbour state that "the condition of permanent enlargement of subinvolution is not due to the non-degeneration of muscular fibre, but to the substitution of connective tissue for the products of this degeneration."

In view of this difference of opinion, and in the lack of positive testimony on either side, it is fair to infer that subinvolution is produced in both ways, the precise process being determined in any given case by the acting cause. In either case the final result would be the same, the method of its production having been minutely described by Dr. Mary Putnam-Jacobi,[6] as a structural alteration in the walls of the enlarged blood-vessels, "in virtue of which nutritive transudations of an albuminous

plasma took [*take*] place, which gradually caused [*caused*] a local development of connective tissue (perivascular sclerosis)." This process she claims to be inflammatory in its nature.

Etiology.—In entering upon the subject of the causation of subinvolution, we are at once in a wide and important field for discussion—wide because of the multiplicity and variety of the causes alleged, important because of the necessity for their recognition and consequent avoidance or removal. The first and most fruitful source of subinvolution is without doubt laceration of the cervix. There are some who still dispute this fact, but their number is rapidly growing less, and it is to be hoped that before many years there will be as great unanimity in asserting the necessity for closing lacerations of the cervix uteri as there is now in urging repair of the perineum after injury.

The testimony of Emmet in this matter may be considered somewhat biassed, yet the accuracy of his observation and the truthfulness of his statement can hardly be called in question. He says[7]: "In closing this brief chapter, I would state that, for many years past, I have met with few or no cases of subinvolution which were not due to laceration of the cervix." T. A. Reamy, in the "American System of Gynecology," pointedly remarks "that if a laceration of the cervix is observed, more or less subinvolution, either of the whole uterus or of the cervix alone, is almost absolutely certain."

The means by which the result is produced are not difficult to understand. In the first place the presence of an open wound, and, later on, of either a mass of cicatricial tissue or an everted and eroded surface of mucous membrane, serves as a constant source of irritation to keep up an active hyperæmia of the uterus. However, in the early weeks, the very effort of nature to repair the damage is opposed to the process of involution, and subsequently, as the wound remains and the irritation persists, the permanence of the hypertrophy is insured by the development of an endocervicitis and an endometritis. It is not necessary that the laceration should be a large one, for even very superficial tears, if exposed to the deleterious influences of an irritating vaginal discharge and denied, by the restlessness or too early effort of the patient, the quiet needed for repair, may fail to heal kindly, and so produce the same result as the deeper lesions —at least so far as our subject is concerned.

Septic absorption is, without question, a far more frequent cause of subinvolution than will be admitted by the mass of practitioners, and a present shame it is, in this age of preventive medicine, that this statement should be true. Not that in every case of subinvolution due to this cause there should have been a well-marked run of "puerperal fever" so-called; but where antiseptic, or at least aseptic, methods are despised or neglected, nothing is more common than to have, during the first week of convalescence, a rise of two or three degrees in the temperature (commonly called milk fever), the presence of fœtid lochia, and moderate abdominal tenderness. In many of these cases there is set up a sufficient degree of uterine or peri-uterine inflammation to interfere seriously with the process of involution; and if this be true of these mild cases, much more surely will subinvolution follow the more marked instances of septic intoxication. Given a case of puerperal septicæmia, and subinvolution may be confidently predicted.

The next cause to receive attention ought perhaps to have been given precedence over the last. It is the faulty management, or rather the mismanagement, of the period of convalescence; and by mismanagement I mean the permission of too much freedom in movement and of too early rising. I am well aware of the fact that patients are not only allowed to be up and dressed before the end of the first puerperal week, but that such a course is even advised by men who are otherwise safe and skilful practitioners and good observers. That the reasons which they give for such a custom have some weight is not denied, but it is far from true that the custom is either a safe or a desirable one. The general weakening and loss of tone of the muscular system, due to a stay in bed of three weeks' duration, is far more than compensated for by the complete rest of the nervous system and the diminution in size of the soft and heavy uterus. The emptying of the uterus and vagina of clots and lochial discharge can be better accomplished by ergot and a douche than by sitting up upon a chamber vessel or chair as advised and practised by Goodell, and without the danger of the latter course.

Another frequent cause is the nervous condition.

Bennett[8] says that he believes that, in subinvolution, the nervous power is so altered in its constitution that vascular congestion of an immoderate amount is permitted, which in itself further increases the trouble by paralyzing the nervous control over the emptying channels, the loose cellular tissue of the late pregnant uterus being well suited for such lesion to occur in. And then we must consider the rapidity of its growth, the enormous distention of its walls, the pressure both from within and from without which it has to bear, as well as the nervous shocks conveyed from mental impressions.

It is a well-known fact of physiology that if a nerve has been bruised or injured between the point of irritation and the muscle, such an injury will often be followed by defective nutrition of the part supplied. We have injuries here which may pass unseen, due to the long-continued pressure of the fœtal head in tedious labors—especially where the delay is in the first stage—the division and bruising of the nerves causing a subsequent loss of function.

The way in which subinvolution is caused by early exertion, and especially by a too speedy assumption of the upright posture after labor, is by the production of displacement of the uterus, prolapse, version, or flexion, and consequent interference with the local circulation, and hence with the process of fatty change and absorption. The uterus remaining large, the displacement continues and increases, the hyperæmia is perpetuated, and the chronic changes already outlined proceed to their full accomplishment. By far the safest course is to take conservative ground, and insist upon a sufficiently prolonged rest in the horizontal posture to permit of a near approach of the uterus to its normal size, and then to make a gradual and cautious return to the ordinary habits of life. The rule of Tarnier is a good one, and certainly does not err on the side of conservatism. Provided the uterus cannot be felt above the pubis, the lochia are no longer bloody, and no fever exists, he permits his patients, between the fifteenth and twentieth days, to be moved to a reclining chair where at first they remain only one hour. The time being lengthened by one hour daily, in three or four days they are ready to try a few steps, and so gradually to gain power to walk without fatigue or injury.

Very painful and tedious labors, by leaving the patient in a state of complete exhaustion from which recovery is slow and uncertain, are probably not infrequently the cause of subinvolution. In this case there is a lack of tonicity in the vessels, the active process of removing the waste and building up the new uterus is imperfectly carried on, a passive hyperæmia persists, and the disease is gradually developed. Severe hemorrhage, either before or after delivery, would act in the same way, by lowering the vital powers and by diminishing the oxidizing properties of the blood.

If the subinvolution is due to hypertrophy of the decidua or to retention of parts of the placenta, membranes, or clots, these should be removed by the use of the curette. Placental adhesions form a source of especial danger, for they keep up an irritation which causes a localized subinvolution, and this in turn has a tendency to become general.

Various other causes have been suggested, such as incomplete emptying of the uterus at the completion of labor, the presence of tumors in or about the uterus, and sexual excitement due to too early intercourse, or even to sharing the same bed by husband and wife. It is to this latter cause, doubtless, that not a few cases of puer-

peral hemorrhage may rightly be attributed; and it is therefore fair to assume that it is capable of setting up a sufficient amount of pelvic congestion to render subinvolution likely.

As predisposing causes may be mentioned a poor state of health from whatever cause, frequent and rapidly recurring pregnancies, and abortions.

Frequency.—For some years after Simpson first called attention to the "Morbid Permanence of the State of Puerperal Hypertrophy," occasional cases were reported from various quarters, but the condition was considered to be an infrequent sequel to pregnancy. Of late years, however, with improved methods and more exact knowledge in the matter of gynecological diagnosis, subinvolution is found to be one of the commonest of the morbid results of childbearing. If it be true that the above-mentioned causes are apt to produce a "morbid permanence of the state of puerperal hypertrophy," then it is by no means to be wondered at that subinvolution is a frequent condition among parous women. It is impossible to give statistics of any value on this point as, in the nature of the case, they must vary materially in the practice of different men, in hospital and in private practice, and also because of the confusion in nomenclature and classification.

The condition once established, from whatever cause, it tends to develop into the more intractable, and oftentimes incurable, disease already referred to as chronic metritis, or areolar hyperplasia; hence the importance of the early recognition of the danger, that the cause may be removed and complete involution secured at the proper time. This point will receive more particular consideration under the head of treatment.

Symptoms.—The history of the case from the patient's own lips indicates that the commencement of the trouble began at a previous confinement. Frequently there has been a previous attack of puerperal sepsis, peritonitis, parametritis, or evidence of some form of septicæmia. Post-partum hemorrhage is often a precursor of this condition.

Such patients almost always complain of backache, and this may be the chief cause for which treatment is desired. There is almost always some disturbance in the menstrual function. This is usually an irregularity indicated by a menorrhagia, a condition in which the periods are of longer duration and come more frequently than is normal. Metrorrhagia may be present often in connection with menorrhagia, and the result of the latter may be so profound as to produce an excessive anæmia. Dysmenorrhœa is often present, due to the engorgement of the already enlarged uterus, which also causes the severe pain. Leucorrhœa, although not always present, may be an accompanying symptom. Its presence, however, denotes an inflammation of the endometrium rather than a simple subinvolution. In weak and debilitated patients there is usually amenorrhœa.

Pain is a very uncertain symptom. Headache is sometimes present; it is referred especially to the crown of the head and is burning in character, occurring at or near each catamenial period. Pain is also localized in the pelvic region, but may be referred to more remote parts of the body, such as the back, hips, legs, and also the breasts. The pain is not of so severe a type as that of chronic metritis.

When the uterus is large and heavy and retroverted, as is often the case, there may be persistent constipation, which usually results in hemorrhoids. Vesical tenesmus may exist from pressure on the bladder or from dragging upon that organ.

The physical signs are especially valuable when acquired by a careful examination. The uterus is found to be soft, flabby, and symmetrically enlarged, more globular in form than normal, and is often displaced. The cervix is also large, with usually a laceration, and the os is patulous, often permitting the entrance of a finger as far as the internal os. The sound passes to a greater depth than normal, and is quite easily moved about; its introduction may cause a profuse bleeding.

Diagnosis.—It is by no means a simple and easy matter to make a positive diagnosis in any given case, unless the patient has been under continuous observation since the pregnancy from which the condition dates, for the reason that the term is rather expressive of a clinical fact than of a pathological process. The uterus may have undergone a perfect involution, the hypertrophy developing subsequently as a result of an endometritis, of a displacement, or of ovarian disease. A probable diagnosis may, however, be made in most cases by a careful comparison of the symptoms and physical signs, the former having dated from a previous confinement or from a period not long thereafter.

On account of the softness and moderate sensibility of the uterus in many cases, the condition may be mistaken for pregnancy in its early weeks, or *vice versa*. In case of doubt, it is far better to wait for time to indicate the true diagnosis than to run the risk of producing abortion by passing the sound. This word of warning is not an idle one, for the accident has often happened to the impatient and thoughtless, and should be guarded against by excess of caution. It is not impossible that the two conditions may coexist, and this possibility furnishes an additional cause for care.

In view of the uncertain relations existing between subinvolution and chronic metritis, and because, if they be separate diseases, the treatment of each is the same, it is hardly worth while to attempt a nice discrimination. If the disease be subinvolution pure and simple, with no metritis or "perivascular sclerosis" grafted upon it, the uterus will be softer and more doughy than normal, will measure three inches or more in depth, and pressure upon it will be easily borne. Where there exists the condition described as chronic metritis or areolar hyperplasia, the uterus is hard and sensitive, and there is usually more or less constant pain in the hypogastric region. The uterus is movable in both conditions, unless there be adhesions or accompanying perimetritis.

Fibroid tumors increase the bulk of the uterus and elongate its cavity, but they can almost always be felt as local enlargements of the uterine mass, or at least the enlargement is not uniform. The history of the case will usually fail to show any causative relation of pregnancy. The appearance of the cervix will often be of assistance, it being usually of normal size and density in the case of tumors wholly confined to the uterine body. Malignant disease confined to the body of the uterus might be mistaken for subinvolution on account of the tendency to hemorrhage, the uniform enlargement, the lack of pain, and the absence of sensitiveness commonly noted in the early months. The age of the patient, the continual presence of a watery discharge, and sometimes the offensive odor, together with the wasting strength, should suggest the nature of the disease, and microscopic examination of shreds removed by the curette will determine it.

Prognosis.—The prognosis of simple subinvolution which has not yet progressed to the sclerotic stage is good, provided suitable treatment be adopted. When the condition is allowed to go untreated, its tendency is to run through the several stages of fibrous deposit, in duration, contraction, atrophy. Under these conditions its course is very variable, being influenced by a great number of factors. In some instances the complete course outlined above appears to have been run through inside of a year, yet on the other hand there are cases which seem to remain almost stationary for years. When the stage of fibrous infiltration has been reached—and most cases presenting themselves for the relief of symptoms have already entered upon it—the prospect of complete cure and restoration to the normal is poor. As a rule, the most that can be expected is the relief of the principal symptoms, partial reduction of the existing hypertrophy, and the avoidance of more serious complications. The uterus may also be placed in a more favorable condition for the occurrence of pregnancy, and for its successful completion.

Treatment.—To a very considerable extent subinvolu

tion is preventable, and hence prophylactic measures should be first considered, and uniformly practised. It is unnecessary to urge the importance of having every woman approach her confinement in the best possible state of health. Of course existing disease will be combated and removed so far as possible, but let the physician also set his face against every depressing influence so often invoked by women to diminish the size of the fœtus and thus to insure an easier labor. Let good diet, fresh air, and plenty of exercise be invoked to aid in establishing or continuing a condition of vigorous health previous to delivery.

The importance of insisting upon a recumbent posture and absence of effort during the first two weeks, and upon a gradual and cautious getting up after labor, has already been referred to.

As septic causes have much to answer for in the production of the disease in question, they must by all means be guarded against, and with the present light upon the subject of aseptic midwifery there is no excuse for the man who neglects such simple precautions as are universally agreed upon. In this connection Goodell[9] says: "The day is surely coming when, to have a case of puerperal fever in one's private practice, will be deemed a crime."

Tedious and very painful labors being, by their exhausting influence, factors in causing, or at least in favoring, the occurrence of subinvolution, they should be avoided so far as possible by the use of forceps and of the various anæsthetic agents. Chloral during a long first stage is capable of giving rest and relief from pain, with proportionate lessening of exhaustion. Ether and chloroform properly used are perfectly safe, and they can be given, if necessary, for long periods without materially delaying the progress of labor, and even with the effect of shortening the duration in many cases. Furthermore, they diminish rather than increase the risk of hemorrhage, and in almost every instance they diminish the severity of the suffering, reduce the fatigue to a minimum, render the convalescence more speedy, and insure a more rapid and certain involution. There is less need of commendation of the forceps, yet if the baneful influence of an unnecessarily prolonged second stage be borne in mind, it will be acknowledged that no mere prejudice against operative interference should be permitted to prevent the timely employment of this means of abridging wear and tear.

Lacerations of the cervix having been shown to result almost inevitably in subinvolution, it follows, as a corollary, that the presence of such tears should always be sought for after labor, in order that this and other possible consequences may be averted by suitable treatment addressed to the lesion. Conversing with a successful fellow-practitioner recently upon this subject, I was assured that not one physician in a hundred makes a practice of examining his patients during or at the close of the puerperal month, and that such a custom is uncalled for. If this belief is general and the former assertion correct, and I believe them so to be, the frequency of subinvolution is to a large extent accounted for. He is a bold man who will fly in the face of such unanimous testimony as now exists to the contrary, and assert that laceration of the cervix is not liable to result in subinvolution, or that it matters not if it does, as the latter condition is one of no importance; yet one of these positions must be taken by the man who disbelieves in the practice of examining his puerperal patients before permitting them to pass from his hands. Unless some special symptoms seem to demand interference, it is well not to examine until after the completion of the second week, and better still is it to wait until the close of the third week, or even of the puerperal month. By this time involution should be well advanced, and the cervix should have returned nearly enough to the normal to enable one to judge well as to the extent of any laceration, should one be present. The treatment of such lacerations needs no consideration here, as this branch of the subject has been fully covered in another article; but the importance of caring for them at an early date cannot be too strongly enforced.

When the examination is made as recommended, any other existing condition which may serve as a possible cause of trouble can be noted and will receive due attention. It is taken for granted that any rupture of the perineum has been previously sutured, but the success of the operation is now to be assured. If the uterus is displaced, it must now be returned to its normal position, and sustained there by glycerin tampons or a pessary.

When subinvolution is discovered soon after labor, simple removal of its causes will usually suffice for a cure. Later on, when the patient applies for treatment for the relief of symptoms, the problem is by no means so simple. Measures directed toward the elevation of the general tone of the system are always called for. Tonic remedies, liberal diet of the right sort, general sponging followed by brisk rubbing, and, in those cases in which suitable exercise cannot be taken, the employment of massage, are to be advised. It being assumed that we have removed all existing local conditions which may serve to perpetuate the disease, our efforts must be turned more directly to the removal of hypertrophy and the restoration of function of the diseased organ.

In almost all cases there exists hyperæmia, which is, indeed, the important element in the continuation of the trouble. This should be attacked by puncture, by scarification, or, better still, by the application of leeches to the cervix; the use of glycerin tampons and of hot douches also aids in reducing hyperæmia. If hot douches are to be of any value, they must be administered while the patient is lying upon her back, with her hips raised; the temperature of the water must also not be less than 110° F., and the douching should be continued for at least fifteen minutes. Painting the cervix with Churchill's tincture of iodine can do no harm, and is often of great benefit. In those cases in which the cervical canal is patulous, and active endometritis is absent, the application of iodized phenol to the uterine cavity by means of an applicator is of marked utility. Such an application should be made about once a week.

Electricity is highly recommended by many writers of recent years, and it has given good results where other means have been tried in vain. Both the galvanic and the faradic currents are of value, either separately or in combination. The faradic current is chiefly available, in recent cases, for promoting contraction of muscular fibre and diminution of hyperæmia. The galvanic current finds its most important application in the later cases, in which fibrous deposit has already taken place.

Massage[10] has not as yet formed an important factor in the treatment of subinvolution, but there are men who advocate its use very strongly. If no contraindications exist, massage may be employed to the best advantage in the first stages of subinvolution, when the uterus is hyperæmic, and when it is found low down in the pelvis, tender, spongy, and having a doughy, elastic condition. If there is an accompanying retroversion this treatment is not precluded; but when the uterus has become hard and firm and has lost its soft spongy feel, massage is useless.

Not infrequently there coexists with subinvolution, or springs up in consequence of it, a condition of hyperplastic endometritis, which is largely accountable for the hemorrhagic symptoms. In such cases it may be necessary to remove the diseased membrane by the use of the sharp curette, following it, in intractable cases, by the application of tincture of iodine, or even of iodized phenol. This, of course, is to be regarded as a surgical operation, strict aseptic precautions being observed, and the patient being confined to bed for several days thereafter.

In some refractory cases of subinvolution, operative interference has been practised by Reamy and others. This consisted in "removing a wedge-shaped piece from the cervix, and closing the rent with sutures as in trachelorrhaphy, . . . when laceration of the cervix did not exist." Good results are reported from this operation.

When a patient has advanced beyond the puerperal state and subinvolution still persists, notwithstanding all our efforts to remedy the condition, relief may be looked for in pregnancy. If the patient becomes pregnant the uterus may, in its natural evolution and in its subsequent involution, if no contrary condition hinders, return to its natural size again.

Subinvolution of the Vagina.—In the vagina, as in the uterus, the process of hypertrophy and development continues throughout pregnancy, to be followed after delivery by a process of involution almost identical in its method and purpose with that which occurs in the uterus. By this means the vagina is restored, in about two or three months, very nearly to its normal nulliparous condition, remaining permanently, however, a little larger than before. This perfect result is, unfortunately, by no means always accomplished, and subinvolution of the vagina is, like subinvolution of the uterus, of common occurrence.

The causes of incomplete involution of the vagina are, for the most part, those that have already been assigned as factors in the production of uterine subinvolution, the latter almost always being accompanied by more or less vaginal subinvolution. The cause which most uniformly and certainly interferes with the process of involution in the vaginal walls is, without doubt, laceration of the perineum or pelvic floor. While laceration of the perineum in its entire thickness is common, laceration of the posterior vaginal wall, together with the inner portion of the perineal body, is, if possible, a still more frequent accident, and is followed by more disastrous results. When a rupture extends through the fourchette, and even more deeply into the skin of the perineum, the injury cannot fail to be noticed by the most casual observer; but when internal inspection is necessary to disclose the rent the chances are strongly against its discovery. The average physician considers his duty done when he inspects the perineum externally, and to his great satisfaction finds that "not even the fourchette is torn," forgetting or not knowing the fact, so strongly insisted upon by Mathews Duncan, that the point at which laceration usually, and in primiparæ almost inevitably, begins is at the ostium vaginæ, not at the ostium vulvæ—at the plane of the hymen, not at the fourchette. In examining the perineum after labor, therefore, look carefully to the mucous surface.

Prophylactic methods of treatment will be the same as those outlined above for subinvolution of the uterus, especial stress being laid upon the care of the perineum both during and after labor. Curative treatment, after known or possible factors in the production of the disease have been removed, will consist in the use of douches, occasional applications of iodine, with insertion of glycerin and alum tampons, and the employment of electricity. While both the faradic and the galvanic currents are of utility, and many prefer the latter, my own preference is strongly for the former. By the employment of a bipolar electrode active contraction of the muscular fibres is brought about, their tone is thereby improved, passive hyperæmia is removed, absorption is stimulated, and the uterus is more firmly supported.

Operative interference is often called for to repair old injury to the perineum or cervix, to remove cystocele and rectocele, or to narrow and shorten a redundant vagina, which, by the simpler means mentioned, cannot be reduced to the normal.

III. Superinvolution.—Nominally, superinvolution is an excess of involution, by which the uterus is reduced to less than its normal size, yet it is an open question whether just this process really occurs. Undoubtedly cases are noted, and with increasing frequency, in which, at some time after the completion of puerperal convalescence, the uterus is found in a state of atrophy; but is this atrophy due to excess of the normal process with failure in the regeneration of muscular fibre; or is it not rather fibrous contraction following upon actual inflammation or occurring as a sequence of subinvolution; or, finally, is it not possibly a result of disease of the ovaries by which their function is destroyed, and hence corresponding to the senile atrophy of the menopause? The present attitude of the profession toward this disease is one of observant scepticism. It is too soon for any one to assert dogmatically that superinvolution, pure and simple, does not exist; yet before making that diagnosis in any case it would be well to consider carefully if there be not some other disease of which the atrophied uterus is merely an expression or consequence. Even the classical case of Simpson—the case which first suggested to his mind the title under consideration—is more likely to have been one of premature atrophy and cessation of function due to tuberculous disease.

But whatever opinion may be held concerning the accuracy of the term, it must be admitted by all that uterine atrophy does occur, without apparent cause, in a certain number of cases, not long after delivery, and to this condition has rightly or wrongly been given the name superinvolution. That the condition is a rare one is shown by the scarcity of reported cases, and by the fact that most writers upon the diseases of women ignore the subject completely.

As regards the pathology of superinvolution, it can only be said that the uterus resembles that organ in a state of senile atrophy. Observations are too few to afford any definite information concerning the morbid processes involved.

There are no distinctive or constant symptoms which belong to the disease, with the single exception of amenorrhœa, or scanty menstruation. Besides this, there is the ordinary train of symptoms common to many another form of uterine disease. Examination reveals simply a non-sensitive uterus, of less than the normal size and depth. The ovaries, if found at all, are commonly much smaller than normal, and are not infrequently bound down and compressed by adhesions.

The disease is a very intractable one, though the prognosis will vary in accordance with the pathological conditions which stand in causative relation to the atrophy. In some cases, diagnosticated as superinvolution, a cure has been achieved and pregnancy has followed; but it may be laid down as a rule that most cases will prove absolutely rebellious to treatment, and sterility will be permanent.

The only treatment which has been found of value is one having for its purpose stimulation of the uterus, and this is best accomplished by the conjoined use of moderate cervical dilatation and electricity. Either a Hanks or a steel-branched dilator may be used to stretch the cervix slightly every week or ten days. Rockwell recommends that both the faradic and the galvanic currents be utilized, and relates one case in his own practice in which menstruation was thus induced in a patient whose uterus measured but one and three-quarter inches. The poles of the faradic battery may be used indifferently, but when the galvanic current is employed Rockwell advises that the negative pole be placed within or against the uterus.

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Revised by *Eugene E. Everett.*

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UTERUS, VAGINA, ETC., TUBERCULOSIS OF.—The relationship between tuberculosis of the uterus, vagina, and vulva, and tuberculosis of the Fallopian tubes, ovaries, and peritoneum, is so close that in the general consideration of the subject it will be necessary to make reference to tuberculosis of the structures above the ute-

rus, which subjects do not strictly belong to this particular chapter. (For a full consideration of tuberculosis of the uterine appendages and peritoneum see the articles on *Fallopian Tubes, Diseases of*; *Ovaries, Diseases of*; and *Peritonitis, Septic and Tuberculous* [in the Appendix].

General Considerations.—Tubercle bacilli gaining entrance to the circulatory systems of the body show what appears to be an elective preference for certain organs. Thus, in the order of frequency, it is found that the involvement affects the lungs, lymphatic glands, mucous membranes, serous membranes, bones, spleen, kidneys, adrenals, brain, genital organs, bladder, and skin. Age has an influence upon the relative susceptibility of the organs, the lungs being most frequently involved in adults, and the lymph glands, bones, joints, and meninges in children. In the female organs of reproduction the order of the frequency of involvement is: Fallopian tubes, uterus, ovaries, vagina, cervix, and vulva. As tuberculosis of these parts is frequently overlooked or mistaken for other lesions, this order may be subject to later modifications. Tuberculosis of the genitals is nearly seven times more frequent in women than in men. Gonorrhœal and other chronic inflammatory conditions appear to increase the susceptibility of the generative organs to tuberculosis.

That the more frequent involvement of certain parts of the body over others is due less to the portal of entry than to differences in the relative susceptibility of the organs themselves, is indicated by the observations made upon lower animals that have been infected by subcutaneous inoculation, intravenous injection, ingestion or inhalation of the bacilli. In such animals a tendency of the bacilli to grow more frequently and more luxuriantly in certain organs is observed. The susceptibility of a particular organ obviously is modified by the degree of general resistance to tuberculous infection possessed by the individual, and by the virulence of the special bacilli concerned. Against the most virulent forms of the tubercle bacilli it is probable that no man and few organs are immune, while other species of the micro-organisms are so attenuated as to be able to produce disease only in persons of greatly enfeebled resistance, and then only in the more vulnerable organs.

Although it is probable that the organs most frequently involved, such as the lungs and lymph glands, are, as a general rule, most susceptible, it is not improbable that in certain individuals the order of the relative resistance of the special organs varies. In this way may we explain the occasional primary colonization of tubercle bacilli in the female genital organs, despite their entrance into the body through the digestive and the respiratory tracts, or through some other remote portal. In such instances it may be that no lesion marks the point of entry of the bacilli, nor the channels traversed by the micro-organisms in passing to the reproductive organs.

Character of the Infection.—Much stress has been placed upon the question as to whether the lesion in the genital organ be primary, or the initial tuberculous focus in the body, or secondary to some other lesion in a contiguous organ or in a distant part from which the bacilli have been carried by the blood- or the lymph-stream. Practically, however, the secondary character of the disease of the genitalia has little influence upon the treatment in the case, provided that the primary lesion be of a trifling character. Far more important is the determination of the dominant, determining, or dangerous lesion in the body. Thus, a tuberculous uterus or ovary, whether primary or secondary, rarely requires the attention of a gynecologist in the presence of advanced pulmonary disease, yet is of great importance when the lesion elsewhere in the body, even though it be primary, is slight and stationary in character.

More important than the primary or secondary nature of the disease—for this may have little influence upon the treatment—is the consideration of the mode of entry of the bacilli, which concerns the prophylaxis against these lesions. As a rule, however, the portal of entrance is difficult to determine, as the bacilli may pass through the mucous membrane and traverse the lymphatic or blood channels without leaving any gross or microscopic evidence of their path. Again, evident primary lesions may indicate the portal of entry.

The bacillus may enter directly through the external genitalia, a condition known as *ascending* infection, or through contiguous organs and remote portions of the body, by means of the blood- or the lymph-stream, designated as *descending* infection.

Mode of Infection.—Ascending infection may occur through contact with contaminated fingers or utensils. Thus, a consumptive may reinoculate herself by sputum carried on her hands, while the more serious danger of initial infection may attend the ministrations of a careless tuberculous physician, midwife, or nurse.

While it is difficult to offer the convincing evidence of concrete instances, the possibility of infection in coitus from disease of the genito-urinary organs, or from the use of tuberculous sputum as a lubricant, is to be considered. The descending form of infection is much the more frequent, although usually it is as difficult to determine the precise portal of entry as it is to give absolute evidence of the primary nature of the lesion. It is apparent that for the most part this will remain suppositious.

The bacilli may be directly carried in the blood or lymphatic vessels from the mucous membranes of the respiratory, digestive, or urinary systems, or from surface lesions of the skin, to the pelvic organs. Often primary lesions mark the path of the invaders, and not infrequently the genitalia are infected by proximity to tuberculous organs, such as the intestines and bladder, or because their peritoneal covering shares in a generalized tuberculous peritonitis.

Character and Frequency of the Lesions.—The lesion may appear in the form of either gray or yellow miliary tubercles, cheesy or puriform foci, masses of imperfectly organized peritoneal exudate, granulation tissue, or chronic ulcerations of the mucous surfaces. The liquid exudate may differ from other inflammatory peritoneal effusions in the presence of small numbers of polymorphonuclear leucocytes and of fibrin, and the presence of many mononuclears and the tubercle bacilli. Most frequently the disease occurs in the form of miliary tuberculosis of the pelvic peritoneum, and is but a part of a more generalized process. At times the tubercles, which appear as slightly raised, firm, grayish or yellowish nodules, from 1 to 3 mm. in diameter, are limited in their distribution to the peritoneal covering of the uterus and its appendages, and may or may not be associated with pelvic exudate and adhesions.

The Fallopian tubes are affected more frequently than any of the other reproductive organs. Besides the form in which only the peritoneum is involved, there is the interstitial type, in which the tube shows a great thickening of its walls, the presence of tubercles, and at times of a serous inflammatory œdema in the muscular walls. Finally, the chief involvement may be the mucous lining, which may show miliary tubercles, or, if the process be advanced, ulceration, or the mucous lining of the tube may be entirely destroyed and the organ greatly distended by a puriform or caseous material. This resembles a pyosalpinx, but the microscope shows the fluid to consist largely of necrotic substance rather than of pus. There is also less tendency for the ostium to become closed than in other forms of salpingitis.

The tube may contain many ounces of fluid, giving it an enormous size. Localized collections of a more or less puriform fluid, walled by masses of exudate and adherent organs, may be mistaken for ovarian cysts. The ovary may be infiltrated by tubercles or distended by large necrotic and cheesy foci.

In the uterus, apart from the miliary tuberculosis of its peritoneal covering, the disease chiefly attacks the endometrium. Miliary tubercles, ulcers, or, when the process is more progressive, the destruction of the endometrium and adjacent muscularis, and the distention of the

uterine walls with caseous material, may occur. This process usually begins in the fundus, and may be especially marked at the cornua. Rarely does it pass the internal os. In the early stage a fine nodular roughening of the endometrium may be detected, but this may be indistinct, and a precise diagnosis is possible only after microscopic study. Later, irregular ulcers with yellowish necrotic bases and edges infiltrated by tubercles may be formed. A diffuse caseous necrosis with a complete destruction of the endometrium is the most common form in the uterus. It may occur in childhood, in middle or in advanced life. The internal os may be obstructed, and the process at times advances to the point of causing a perforation of the muscular wall of the uterus. Rarely there may develop in the uterus a pure interstitial or muscular form that may progress until it produces a perforation into the abdominal or uterine cavity. Early in the process such an involvement may predispose to uterine rupture during pregnancy or labor.

Primary tuberculosis of the uterus is very rare. It is usually secondary to tuberculosis of the Fallopian tubes or to phthisis pulmonalis. As a secondary condition it is not uncommon, and in such cases the tuberculous process is usually limited to the corpus, the cervix being healthy. On the other hand, in the rare cases in which the cervix is attacked, the corpus is usually normal. Merletti (*Archivio di Ostet. e Ginec.*, December, 1901) states that in one hundred and seventy-two cases of genital tuberculosis, seventy-five had the uterine body affected.

Tuberculosis of the cervix usually proceeds to the formation of ulcers or fungating papillary masses. The ulceration may extend over the vaginal portion of the cervix, the base of the ulcer showing reddish granulations and a superficial mass of caseous necrosis. Minute, firm, grayish or yellowish tubercles may be present throughout the surface of the ulcer or in the adjacent tissue. In the papillary form masses occur within the canal, and the clinical picture resembles that of carcinoma. There is, however, less bleeding on manipulation, and the induration is less wooden. Tuberculosis of the cervix is very rare. The first case was described by Virchow ("von Rud. Tuberkulose der Scheide," *Virchow's Archiv*, Bd. v., p. 404). In the majority of cases of cervical tuberculosis, tuberculosis of the vagina has been present. Tuberculosis of the corpus seldom exists in conjunction with tuberculosis of the cervix. J. Whitridge Williams ("Tuberculosis of the Female Generative Organs," Johns Hopkins Hospital Reports, 1892, vol. iii., p. 85) was able to collect only seven cases. It is probable that certain cases of tuberculosis of the cervix have been diagnosed as instances of cancer, thus forming a possible source of error in estimating the permanent results of hysterectomy for cancer of the cervix.

In the vagina and upon the labia miliary tubercles and irregular ulcers with indurated yellowish or reddish bases and thickened borders have in rare instances been noted. In the vagina the posterior wall is the seat of election for the disease. Tuberculosis of the vagina is usually secondary to tuberculosis of the higher portions of the genital tract, though it may occur independently of any tuberculous infection of the rest of the genitalia. Tuberculous ulcers may perforate the wall of the vagina and, according to their location, lead to the formation of recto-vaginal and vesico-vaginal fistulæ.

The lupus occurring upon the vulva resembles that which occurs upon other portions of the body. The vulva is less often the seat of tuberculosis than any portion of the genitalia. J. Whitridge Williams ("Tuberculosis of the Female Generative Organs," Johns Hopkins Hospital Reports, 1892, vol. iii., p. 85) was able to collect only three cases in which the diagnosis, based upon microscopic and bacteriologic examinations, was undoubted. Many cases of supposed lupus have been due to syphilis or to non-tuberculous ulceration.

It seems probable that the supposed rarity of the disease below the Fallopian tubes is due in part to the lack of pathologic or bacteriologic study of obscure lesions.

Under the microscope the tubercles found in the genitalia resemble those found elsewhere in the body, frequently combining giant cells and caseous centres with a peripheral zone of epithelioid and lymphoid cells.

Diagnosis.—Cover-glass smears made from the secretions of the uterus or local lesions when properly stained may show the characteristic bacilli. Care should be taken by inoculation experiments, or other tests, to exclude the smegma bacillus.

The most delicate reaction is by the injection of suspected secretion into the peritoneal cavities of guinea-pigs. In from three to six weeks, should virulent tubercle bacilli be present in the secretion, the animals will show a characteristic involvement of the organs. Uterine scrapings, scrapings or sections from ulcers, when sectioned and stained, may show characteristic tubercles or the bacilli. I have observed typical tubercles in bits of granulation tissue scraped from a pelvic sinus. Sections should be made of all excised organs, and, in doubtul cases, inoculation experiments in the lower animals should be carried out.

Clinically, tuberculosis is to be thought of when a marked salpingitis, perimetritis, or endometritis occurs in young children or in adults, provided we can exclude gonorrhœal or puerperal infection. The diagnosis is rendered more probable when tuberculous foci are present in the lungs or other organs. Tuberculosis of the vulva, vagina, and cervix may be suspected when these tissues are infiltrated or ulcerated. The lesions resemble those of tuberculosis upon other mucous structures, but the diagnosis must rest upon histologic and bacteriologic studies. In tuberculosis the adhesions about the Fallopian tubes may be extensive, and yet the ostia of these tubes may not show the same tendency to undergo closure that is observed in other forms of salpingitis. As to the general symptoms, the great disproportion which exists between the marked cachexia and the insignificant amount of local disease is suggestive, while the injection of tuberculin causes a well-marked reaction. The pathologic process is aggravated by pregnancy, by coitus, and generally by debilitating conditions, especially such as occur in diabetes.

Treatment.—Tuberculosis of the uterus, whether of the corpus or of the cervix, when primary or when secondary to tuberculosis of the uterine appendages or of the peritoneum, should be treated by hysterectomy. Abdominal hysterectomy should be preferred as affording the opportunity of dealing more satisfactorily with the involved appendages and of inspecting the abdominal peritoneum. When tuberculosis of the uterus is secondary to tuberculosis in the lungs or other organs of the body, hysterectomy is still indicated, provided the tuberculous process elsewhere is not extensive and is not progressive, and provided also that the nutrition and vitality of the particular patient is sufficiently good to enable her to withstand a major operation. When tuberculosis of the uterus or cervix is secondary to or complicated by active tuberculosis in other organs of the body, or when the vitality of the patient is too greatly reduced to render a major operation advisable, treatment addressed to the cure or amelioration of the complicating conditions should first be instituted. Admission should be sought in a well-equipped sanitarium for the treatment of tuberculosis; or, if this is not available, the influence of rest, forced feeding, life in the open air, and tonic medication should be advised. During the continuance of such general treatment, should the discharges from the uterus be annoying or offensive, bland aseptic or mild antiseptic vaginal douches should be employed. In cases in which local discharge, whether of blood or of pus, is a marked feature, and in which a radical operation is contraindicated, curettage, with local applications of silver nitrate, iodoform, etc., may occasionally be indicated.

The treatment of tuberculosis of the vagina depends upon the character of the lesions, upon whether they be primary or secondary, and upon the complications in the particular case. Isolated lesions, when not too exten-

sive, should be treated by excision and suture. When this is not feasible, owing to the extent of the lesion or to too great involvement of the recto-vaginal and vesico-vaginal septa, the condition may best be treated by curettage, followed by the application of silver nitrate, iodoform, or other topical applications used in tuberculous lesions of mucous membranes in other portions of the body. In complicated cases in which the involvement of the vagina is but a minor part of a more general condition, local measures should be restricted to those which promote the comfort of the patient by the removal of discharges and the relief of pain.

Tuberculosis of the vulva should be treated by excision, when the lesions are not extensive. In cases in which the tissues are involved to a marked degree, Finsen-light treatment should be employed, this having given excellent results in lupus of other portions of the body.

The importance of general treatment, both in connection with local treatment, addressed to the generative organs and as supplementary to local treatment whether topical or operative, cannot be too strongly insisted upon. It would be better if all cases supposed to be cured of local tuberculosis were treated by the methods which are employed for building up the system and which are considered necessary in the treatment of incipient tuberculosis.

The prognosis of tuberculous cases should almost never be hopeless. Not infrequently the most unpromising cases do well, and sometimes make good recoveries.

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UVA URSI. See *Bearberry*.

UVULA AND SOFT PALATE.—Anatomy.—The soft palate, or velum pendulum palati, is, as its name implies, a movable curtain or fold formed by a duplication of the mucous membrane which covers the hard palate and is continued backward from it. It contains muscular fibres, an aponeurosis, vessels, nerves, and mucous glands, and forms a valve, more or less complete, between the mouth and the pharynx. Its inferior border is free and pendulous, and is prolonged in the middle into a small conical process, *the uvula*. At each side it presents two curved folds known as the arches or pillars of the soft palate, and which, starting from above at a short distance outside the median line, extend downward and outward, diverging in their course to form the triangular space in which lies the tonsil. These folds are called respectively *the anterior and the posterior pillars of the palate*. The anterior descends to the side of the tongue, while the posterior runs downward and backward into the pharynx. The space which is situated between the anterior arches of the palate, and which constitutes the passage-way from the mouth to the pharynx, is called *the isthmus of the fauces*. The mucous membrane covering the greater part of the velum, as well as its free margin, is covered with pavement epithelium. At the upper part, however, and near the orifice of the Eustachian tube, ciliated and columnar epithelium is found. The epithelium of the gland ducts is also, in many instances, of this character. At birth the whole posterior surface of the velum is lined with ciliated epithelium, which later becomes squamous. The soft palate is acted upon by five pairs of muscles, two superior, two inferior, and one intermediate.

The superior muscles are the tensor palati and the levator palati, the two inferior are the palatoglossus and the palatopharyngeus, and the intermediate is the azygos uvulæ.

The tensor palati, or circumflexus, arises from the anterior aspect of the cartilaginous portion of the Eustachian tube, from the navicular fossa at the root of the internal pterygoid plate, from the spine of the sphenoid and the edge of the tympanic plate of the temporal bone; it descends vertically between the internal pterygoid plate and the inner surface of the internal pterygoid muscle, and terminates in a tendon which winds around the hamular process, being retained in this situation by some of the fibres of origin of the internal pterygoid muscle, and lubricated by a bursa; it extends horizontally inward, and terminates in the anterior part of the aponeurosis of the soft palate and the under surface of the palate bone.

The levator palati muscle arises from the under surface of the apex of the petrous portion of the temporal bone, in front of the orifice of the carotid canal, and from the adjacent cartilaginous parts of the Eustachian tube. It passes downward and forward, approaching the median line, and is expanded upon the posterior surface of the soft palate as far as the median line, where its fibres blend with those of the opposite side. Superiorly, it is placed above the concave margin of the superior constrictor.

The palatoglossus muscle (constrictor isthmi faucium) is a fasciculus, narrower at the middle, which forms, with the mucous membrane covering it, the anterior pillar of the soft palate. It arises from the anterior surface of the soft palate, on each side of the uvula, where its fibres are continuous with those of its fellow of the opposite side, and, passing forward and outward in front of the tonsil, is inserted into the side and dorsum of the tongue.

The palatopharyngeus muscle, occupying the posterior pillar of the palate and forming, with the palatoglossus, the triangular space in which lies the tonsil, arises in the soft palate by fibres connected with those of the opposite side, and passing partly above and partly below those of the levator palati and azygos muscles. As the muscle descends it becomes greatly expanded, and its fibres are found extending from the posterior corner of the thyroid cartilage backward to the middle line of the pharynx, some of the fibres decussating posteriorly with those of the opposite side.

The azygos uvulæ muscle (so called from having been supposed to be a single muscle) consists in reality of two fasciculi; these arise from the posterior nasal spine of the palate bone and from the tendinous structure of the soft palate, and descend to be inserted into the uvula. The fasciculi are separated by a slight interval above and unite as they descend.

Diseases.—The diseases of the soft palate and uvula may be classified into two groups, namely, general and local. In the first division may be grouped such as are symptomatic, and merely the local manifestation of a general condition, such as measles, scarlet fever, diphtheria, syphilis, tuberculosis, and lupus. Although the local lesion in any of the above affections cannot compare in importance with the general disease, there may arise certain conditions under which the throat affection may become of decided importance, as will be seen later on in the study of chronic inflammation, diphtheria, and syphilis of the parts. Local affections of the soft palate include the various inflammations which may attack it, such as simple hyperæmia, acute, subacute, and chronic congestion, œdema, and phlegmon, as well as general relaxation, dilatation of the superficial blood-vessels, paresis, new growths, and congenital malformation.

Inflammation.—Acute catarrhal inflammation of the uvula and soft palate presents the following symptoms: The uvula is reddened, swollen, and somewhat sensitive, the sensitiveness increasing at each effort of deglutition, and the patient experiencing a sharp pain, as from the presence of a foreign body in the throat. If the inflammation be severe, œdema of the submucous connective tissue and of the muscular tissue beneath may occur, giving rise to an acute prolapsus of the uvula, and attended with much irritation and discomfort. These anatomical changes are usually temporary, and disappear with the subsidence of the attack. Follicular and herpetic inflammations of the uvula are usually associated with the same condition in the pharynx, and therefore show no features which are distinctive.

Phlegmonous uvulitis is characterized by the greater intensity of the accompanying inflammation. The uvula is very much swollen and reddened, and the pain is excessive. The sensation is as of a heavy, voluminous body in the mouth, which in the act of deglutition gives

rise to lancinating, almost unbearable pain. Respiration, besides, is more or less seriously impeded. In such cases the inflammation involves both the mucous membrane and the submucous connective tissue, and also the azygos muscle, and it may extend to the neighboring parts.

The causes of the above-mentioned forms of inflammation of the uvula are, in general, as follows: Influence of cold, or of irritating substances, such as too hot food or drink, burning or irritating alkaline substances or mineral acids; and, finally, progressive inflammation extending from the neighboring parts. As already mentioned, the symptoms of acute uvulitis do not last long, and the disease can usually be shortened by the application of medicines such as are generally used for similar conditions elsewhere. Sometimes the disease becomes chronic, especially when the inflammation is often repeated, or the patient is suffering from constitutional disease or general disturbance of nutrition.

The chronic catarrhal form of uvulitis presents all the well-known changes in appearance which are common in like affections of the pharynx and larynx. A granular condition of the mucous membrane is especially frequent, originating in a hyperplastic inflammation of the mucous glands. The surface of the uvula is hard, reddened, and covered with small nodules. Between the latter the mucous membrane is indurated, hyperæmic, and insensitive. The condition is often associated with a similar disease of the pharynx, and it occurs most frequently in strumous and anæmic subjects, or in those whose general nutrition has become impaired. It is a somewhat stubborn affection, for which general as well as local treatment is required.

Relaxed Uvula.—Chronic inflammation of the uvula usually ends in prolapse and hypertrophy, a condition which may give rise both to direct and to reflex irritation of a serious nature. One of the chief causes of relaxed uvula or, more properly speaking, of the catarrhal troubles which occasion it, are vicissitudes of climate and variations of temperature, especially in countries where there is a frequent combination of cold and wet weather.

Exposure to night air, or to the vitiated atmosphere of crowded and overheated rooms, overindulgence in eating or drinking, and excessive smoking are among the causes of relaxed throat. It is a common companion of the alcoholic habit, often being associated with the gastric catarrh which attends that condition. Occurring in the morning, it is probably due to mouth-breathing from nasal or naso-pharyngeal obstruction; in the evening, from fatigue. It is often seen in those suffering from general depression, and when it is observed in women in whom uterine disease is present, it is probably the result of the general enfeeblement caused by the latter, rather than of any distinct reflex influence. Marked elongation of the uvula is often present in strumous children and in those in whom the tonsils are enlarged. It is sometimes congenital. In general, any cause which may produce a relaxation of the velum palati may also be followed by relaxation and elongation of the uvula.

The symptoms of an acute attack of relaxed palate are a sensation of fulness and stiffness of the throat, together sometimes with the sensation as of a foreign body. There are also an uncomfortable feeling of dryness, and a desire to make repeated efforts to dislodge the supposed foreign substance.

The symptoms may quickly subside, or they may continue for several days. Examination reveals more or less congestion of the parts, although this is sometimes so slight as hardly to be noticeable. There are also slight swelling, and often a varicose condition of the smaller veins. The elongated state of the uvula may give rise to a greater or less degree of local irritation. Sometimes this becomes excessive, occasioning persistent and severe attacks of coughing. In case the uvula be long enough to touch the epiglottis or the larynx, severe paroxysms of coughing may occur whenever the patient lies upon his back. This may cause him much distress upon lying down at night, and, should he turn upon his back during sleep, may waken him with a sense of impending suffocation. When the condition has become chronic, or is congenital, these suffocative attacks may be of almost nightly occurrence, the patient being obliged to sleep with the head raised by several pillows to obtain any immunity from them. Sometimes the attendant hyperæsthesia of the pharynx is so pronounced that the patient may be subject to sudden fits of violent, spasmodic cough upon the slightest provocation, or even without any apparent reason at all. The writer has seen a case of spasmodic stricture of the œsophagus, in a patient suffering with elongated uvula and hyperæsthesia of the pharynx, which was cured by amputation of the uvula. Again, so great may be the irritation that cough, loss of appetite and sleep, and nausea and vomiting may result in such pronounced emaciation, anæmia, debility, and malaise that the case may, upon superficial examination, be taken for one of phthisis. Indeed this error is not infrequently made.

Proper treatment of relaxed uvula generally results in the cure of the disease. The various exciting causes of the trouble should, if possible, be carefully avoided. The patient should be directed to live in a dry and bracing climate. Indigestion or constipation, if present, should be corrected. Anæmia and debility must be removed by the administration of tonics, and the local condition is to be treated by the application of mild astringent sprays or insufflations. If the uvula be much elongated, if it be a source of irritation, and if it refuse to retract under the influence of local treatment, it should be shortened.

Amputation or abscission of the uvula has been practised among many peoples from a very early date. Although in itself an apparently insignificant operation, it is one of great utility and practical importance.

At the present day uvulotomy is practised with an increasing degree of discretion, as some reproach has been cast upon it by the indiscriminate and clumsy manner in which it has sometimes been performed.

For the more convenient and perfect performance of the operation many instruments have been devised.

By far the simplest and best instrument is a pair of long-handled scissors, having the blades curved sideways toward the right hand, and one blade hooked at its tip so that the uvula may not slip from its grasp. A holder, made on the principle of Sims' uterine thumb forceps, an instrument about eight inches in length, possesses the advantages over other forceps that it has not the inconvenient scissors handle, that it may be held firmly and with great steadiness by allowing its proximate end to rest in the hollow between the thumb and forefinger, the whole hand meanwhile being steadied by resting the fourth and fifth fingers against the patient's chin, and, finally, that in applying the scissors the forceps may be used as a guide.

In operating, the patient's tongue should be held down by himself, or by an assistant, with a tongue depressor. The amount necessary to be removed having been carefully estimated, the uvula is grasped by the forceps at a point below the proposed line of incision and drawn slightly forward. The scissors, carefully guided by the hand and eye of the operator, are then applied, and the separation of the redundant tissue is completed. The same result may be obtained by means of the Jarvis snare, in the use of which it is only necessary to seize the part to be removed in the loop of the écraseur, without the aid of the forceps. This latter method is not painful if cocaine anæsthesia is employed, and it has been found by the writer to be particularly convenient and effective. Should there be any fear of exciting undue bleeding, the galvano-caustic loop may be used, the uvula being first drawn forward as in abscission by the scissors. As was long ago pointed out by Llewellyn Thomas, the line of incision should be directed from below obliquely upward and backward, in order that the wound may be exposed as little as possible in the act of deglutition. Local anæsthesia should always be secured before the operation. For this purpose the holding of a

piece of ice in the mouth for a few moments before the operation is effective and free from the objectionable features of cocaine. Pain during and after the operation will vary greatly in different cases. While in the case of a slender, anæmic uvula it may be very slight, in a thick, congested, hyperæsthetic one it may be severe and annoying, and the process of healing may be protracted for from two days to a week. Morell Mackenzie insists that, where there is any follicular disease of the throat, it is most important to cure that affection before the uvula is amputated, as, owing to the after-pain caused by the removal of the uvula, patients will not submit to any further treatment when they have recovered from the operation. Hence the patient remains uncured, and the operation, and he who performed it, are brought into discredit. The amount of relief, however, which is possible from this apparently insignificant procedure is sometimes remarkable, the whole train of symptoms, local and reflex, vanishing as if by magic, the general health returning to a normal basis, and the voice gaining markedly in quality and power. This, however, is not invariably the case, as the reflex symptoms may be slow in leaving, not disappearing entirely until a considerable length of time has elapsed. This possibility should be recognized and explained to the patient in order that he may not be subjected to unnecessary disappointment.

While the operation of uvulotomy is attended with the slightest possible degree of danger, and the bleeding which follows it is seldom more than a few drops in amount, in certain rare instances hemorrhage, more or less troublesome in its character, has resulted. The existence of an anomalous distribution of the arteries or veins of the velum palati may be an important factor in producing hemorrhage, while excessive hypertrophy or the presence of a varicose or hemorrhoidal condition of the vessels would certainly predispose to bleeding. Operations performed during the existence of acute inflammation, œdema, or ulceration are more likely to be succeeded by bleeding than when made for simple prolapsus.

The character of the bleeding is usually arterial, as is evidenced by the color of the blood, the spurting of the vessels, and the pulsation of the stump. Nevertheless, venous hemorrhage is sometimes noticed.

Troublesome bleeding is not necessarily attributable to the removal of too much of the uvula, for a simple clipping has caused profuse hemorrhage, while extensive removals may be almost bloodless. The existence of the hemorrhagic diathesis would of course exert an influence in rendering bleeding after uvulotomy persistent, although there is not a clearly established case of this nature on record.

The most reliable surgical methods for controlling uvular hemorrhage are the ligature, compression by the clamp or forceps, or the use of the galvano- or the actual cautery.

The most reliable styptics are, in the order named, adrenalin, solutions of antipyrin, tannogallic acid, alum, or the solid silver nitrate, directly applied to the bleeding stump, the local use of ice, ice water, and vinegar.

Ordinarily, the best plan for preventing bleeding is to urge the patient to refrain from attempts at clearing the throat. Should the hemorrhage persist, it may usually be checked by the sucking of cracked ice, or by gargling the pharynx with hot water. Applications of the solid nitrate of silver, or of the galvano-cautery, are also effective, or in severe cases a ligature may be applied to the stump. A device at once simple and effective is the method of applying direct pressure. One of the small spring clamps used in retaining shirt sleeves in position is trimmed down with shears, the spring weakened, and a string attached to a perforation made in one of its arms. The arms of this improvised instrument are widely separated by means of a dressing forceps, and quickly slipped over the uvula and well up on the soft palate; the forceps are then withdrawn, and the clamp remains securely fastened and in the desired position. The teeth of the clamp should be slightly filed down prior to introduction, and the string attached to the [illegible] patient's ear.

Occasionally the operation of uvulotomy is followed by a somewhat slow process of healing, and attended with considerable pain, deglutition becoming almost impossible, and even the swallowing of the saliva causing inconvenience. In such cases the patient should be directed to abstain from such articles of diet as seem likely to increase the irritation. Indeed, it is well in all cases to recommend that bland and unirritating food be taken until the healing process is fairly completed. Gum arabic, or a marshmallow drop allowed to dissolve in the mouth, will give decided relief, while, in case the granulations become exuberant, an application of the solid nitrate of silver will hasten recovery. When much pain is experienced in swallowing, the application of a two-per-cent. solution of cocaine is indicated. Pain reflected to the ears may be annoying. The highest authorities are unanimous in insisting upon the deleterious effects of an elongated uvula upon the voice, and upon the vital importance to that function of remedying the evil.

Malformations of the uvula are not infrequently observed. In addition to asymmetry or absence of the part, two common varieties of detormity are met with, viz., congenital elongation or undue length, and the condition known as bifid or double uvula. In the former the whole structure, including the muscular tissue, is lengthened to a greater or less degree beyond the normal limit, the amount of elongation in some recorded instances being incredible.

Congenital elongation of the uvula has been observed by the writer as an hereditary trait, several members of the same family showing the same condition of general hypertrophy and lengthening. The condition is easily remedied by the amputation of the redundant part.

Bifurcation of the uvula, a result of arrested development, is quite common. It may be regarded as the least possible manifestation of cleft palate, and may occur in any degree, from a slight indentation at the tip of the organ to complete division of it to its base. It often exists without giving rise to symptoms indicative of its presence. When it is attended with much hypertrophy it causes the same abnormal symptoms which are observed in ordinary hypertrophy. Abscission of the redundant portion is effective in securing relief. This, however, is a clumsy method of operation, since, if the bifurcation be extensive, a broad, truncated stump is left. To avoid this, in the opinion of the writer, some attempt at a plastic operation should be made, in order to secure, if possible, the union of the two stumps in the median line. This may be accomplished, in the majority of instances, by first removing the tips of the two uvulæ, and then denuding, with small curved scissors or the galvano-cautery, the inner aspect of each well up to the base.

New Growths.—Papillomatous growths, generally of small size, but sometimes of sufficient dimensions to cause irritation, are occasionally seen upon the uvula. They are usually located near its free extremity and may be either pedunculated or sessile. They are also found independently of any diathesis. Myxomata of the uvula are occasionally seen. Angiomata or vascular growths may also occur.

Occasionally a benign growth may be attached to a pedicle so long that the tumor itself escapes observation until drawn upward and forward. In all of these cases amputation of the uvula above the site of the growth is at once successful in relieving the difficulty.

Malignant growths of the uvula and soft palate are occasionally encountered, usually, however, as an extension of the disease from adjacent parts.

Syphilis, tuberculosis, lupus, and lepra of the velum and uvula are met with, the first often, the last three rarely.

The main points in the differential diagnosis between them are, that in syphilis the various lesions common to this disease are usually disposed upon the soft palate in a markedly symmetrical arrangement, they are but slightly painful, and they yield quickly to specific treat-

ment. Tuberculous ulcers are far less common than the former; they are usually superficial; they often give rise to extreme pain, and they coexist with well-marked disease of the lungs, and generally with other manifestations of ulceration in the pharynx. The differentiation of lupus from syphilis of the soft palate is sometimes difficult, especially if the patient be also suffering from general syphilis. The chief characteristics of lupus are that the normal sensitiveness of the part is maintained; or, if altered, there is anæsthesia. The tubercles are multiple, which distinguishes the disease from carcinoma; they are rounded, their surface is smooth and glistening, and their color is bright red. They are firm in consistence, but less firm than epithelioma. The diagnosis may be confirmed by the presence of external manifestations of the disease. Lesions of the mucous membranes, common in leprosy, never occur until the disease has clearly manifested itself in other parts of the body. As a rule, therefore, little doubt can arise as to the true nature of the pharyngeal disease. Here, as elsewhere, the course of lepra is one of active and widespread destruction.

Syphilis of the Velum Palati.—The occurrence of the primary lesion of syphilis, although now and then observed upon the tonsil, is, upon the velum, almost unknown.

In the secondary manifestations of the disease, however, the soft palate and uvula are frequently involved. The conditions presented are those commonly seen in the adjacent parts of the oral cavity, and include simple erythema or congestive patches symmetrically disposed, submucous infiltration, mucous tubercles, followed by mucous patches, or by the formation of condylomata. A peculiar feature of these manifestations is their symmetry, which, as is often seen upon the uvula, is so well marked as to attract the attention of the observer. Early in the disease the congestion may be so indistinct as to escape observation. Gentle irritation, however, will often cause the distinctive character to be intensified. Considerable rise of temperature often accompanies the first appearance of this form of sore throat.

The tertiary form of syphilis may occur in the soft palate at any period of time beyond two years after the primary infection. It is characterized by true ulceration or loss of tissue, and is the result of the degeneration of gummatous deposit.

The effects upon the velum palati of tertiary syphilis are often most disastrous. A frequent seat of gummatous infiltration, its exposed situation and delicate texture render it liable to serious injury as the result of tertiary ulcerative processes. These are often characterized by extensive loss of substance, and are followed by marked cicatricial contraction and the formation of adhesions between the remaining tissue and the neighboring soft parts, which not only destroy the velum itself and abolish its functions, but result in a closure or a shutting off of the upper pharynx from the lower. This closure is more or less complete in proportion to the extent of adhesion present, and may vary from a slight narrowing of the aperture, due to adhesions at the outside angles of the velum, up to a degree of occlusion which seems absolute. Two varieties of cases may be described: (1) Those in which simple ulceration has taken place, at or near the margins of the velum, without material loss of substance. In such cases, the adhesions being limited to a somewhat narrow band of union between the edge of the velum and the pharynx, and the greater part of the velum itself being intact, the prognosis is good. (2) When the loss of substance has been considerable, and when the soft palate has become extensively adherent to the pharynx, relief becomes a matter of extreme difficulty, and, in many cases, is next to impossible by any known plan of treatment. In the worst cases the whole posterior surface of the velum, and the superior surface of the soft palate, seem to be firmly incorporated with the posterior pharyngeal wall. In these cases the roof of the mouth and the posterior wall of the pharynx seem to be continuous, the line of adhesion not being traceable in the confused mass of cicatricial bands which represent the original structures, and which are sometimes disposed in the shape of irregular vertical digitations, between which there may be one or more places in which the adhesion is incomplete, and through which a probe may be passed. Cases, however, in which complete occlusion has actually taken place are rare. Should the opening be invisible upon inspection of the pharynx, it may generally be demonstrated by forcing air into the nasal cavities by means of a Politzer inflator. If an opening exists, its presence will be indicated by the appearance of bubbles in the pharynx, when the air is forced through the opening.

The results of extensive adhesion of the velum to the pharynx are most distressing, and may be summed up as follows: (1) Mouth-breathing, with all of its attendant evil results; (2) impairment of the quality and tone of the voice; (3) interference with drainage from the nasal cavities and nasopharynx; (4) consequent upon this, loss of hearing from irritation of the Eustachian tube, and from the almost inevitable occurrence of serious middle-ear disease; (5) loss of the sense of olfaction, owing to the lack of a current of air through the nasal passages, such a current being necessary to bring the odoriferous particles in contact with the olfactory membrane. When the passage to the lower part of the pharynx is contracted, there is sometimes dysphagia as well as dyspnœa.

The treatment of this condition consists in the attempt to separate the adherent tissues, and to establish, more or less perfectly, communication between the upper and the lower pharynx. To carry out this design with success is one of the most difficult problems of surgery. Perforation of the velum through the breaking down of gummatous deposits is said to be a cause of serious danger to that organ, since, having thereby lost to a greater or less degree its muscular vigor and resiliency, it is liable to swing backward against the pharynx, instead of being held at a normal distance from it. Furthermore, a perforation renders it all the more liable to form adhesions subsequently with neighboring parts. The mechanism, however, by which adhesion commonly takes place, is the same as that which is observed in the cicatricial union of the fingers of the hand following burns. Despite all possible care, the cicatrizing surfaces begin to unite at the bottom of the angle between the members, and the process of adhesion continues until the denuded surfaces, throughout their whole extent, have become firmly joined to each other.

In the treatment of these unfortunate cases the first care should be to prevent adhesion, by checking with all possible diligence the appearance and spread of ulceration upon the parts. Not only should the iodide of potassium be freely administered, combined if necessary with mercury, but local applications should also be made to the ulcers: of nitrate of silver, or the acid nitrate of mercury, if they be spreading, or of a solution of sulphate of copper (gr. xv. ad ℥ i.) if they be indolent. If this treatment fails, means should be used to keep the ulcerated surfaces apart. For this purpose several methods have been proposed, but as they apply as well to the separation of the parts after operation, they will be described later.

The prognosis as to the results of operation must depend largely upon the extent of deformity present in a given case. Where the degree of adhesion is comparatively slight, the adherent surfaces may be separated by means of a small, flat knife. As, however, the separated parts have a very strong tendency to reunite, it will be necessary, after operation, to use means for preventing such a reunion. Of these the simplest is the application to the cut surfaces of monochloracetic acid. This forms an adherent eschar, under which the healing process seems to progress to such a degree that, when the eschar separates and comes away, the period in which adhesion would have taken place has passed, and the parts heal without uniting.

Few cases, however, are so simple as to render the above method possible. Perhaps the most valuable plan

of treatment yet suggested is to separate the united parts by means of the galvano-cautery, and then to use great diligence in keeping them apart, and in maintaining full dilatation of the passage. This may be done by repeatedly drawing forward the remnant of the velum by means of a palate hook—a procedure which the patient can carry out himself; or, as has been suggested, a piece of tape may be passed through each nostril and out at the corresponding angle of the mouth, the velum being thus drawn away from the posterior pharyngeal wall; or, finally, given the best results, a piece of metal shaped to fit the space between the velum and the pharynx may be suspended from two stout threads passed forward through the nose, and tied so as to hold the plate in position. This, worn constantly, serves as a permanent dilator.

Since readhesion after operation is due to granulation and union at the external angles of the wound, as in web finger, Nichols has devised the following excellent operation: Before attempting the separation of the velum from the posterior wall of the pharynx, openings should be made through the adhesions and at their extreme outer angle, one on each side. These openings should be kept packed until their surfaces have healed. Thus the granulating angle will have been destroyed, and in favorable cases the remaining adhesions can be separated and kept apart with success.

In cases in which the degree of deformity is excessive, the best that has hitherto been accomplished has been to widen the channel of communication between the upper and lower pharynx sufficiently to allow the nasal secretions to be drained away. This has been done by applications of the galvano-caustic knife, followed by persistent dilatation, practised by the patient himself by means of some form of sound. It is highly probable that by the last-mentioned method an opening of considerable size may be maintained. Preliminary to operating upon such a case, much aid may be secured by passing a sound backward through the nose, and demonstrating the lowest and most superficial point of the pharyngeal pouch. By cutting against the point of the sound used as a guide, an entrance may easily be effected.

Finally, it must be said that, although the prognosis as to relief of adhesion of the soft palate to the pharynx is often most unpromising, much may be done to help the sufferer by skill, ingenuity, and unremitting patience in the application of the means already at hand.

Neuroses of the Velum Palati and Uvula.—These may be either sensory or motor. With the former may be classed anæsthesia, hyperæsthesia, paræsthesia, to which may be added vaso-motor neuroses, and, possibly, neuralgia. Motor disturbances include spasm, or increased mobility, and paralysis, or diminished mobility. The causes of these neuroses may be either central or peripheral, and they may be either unilateral or bilateral.

In addition to the central causes which may produce anæsthesia of the velum, it may also be present in epilepsy, chorea, and hysteria. It commonly occurs after diphtheria. It may be caused artificially by certain drugs, among which may be mentioned cocaine, morphine, chloral, and bromide of potassium. The symptoms, if present, consist usually in a feeling of relaxation of the part, or a sensation as of the presence of cotton or wool in the pharynx, sometimes associated with a feeling of pain.

Hyperæsthesia is often met with, and may be due to elongation of the uvula, inflammations of the pharynx, acute and chronic, the presence of a new growth, or a dilated condition of the blood-vessels.

Neuralgia seems to exist in certain rare cases, in which, without apparent cause, lancinating pain is experienced, and areas of localized tenderness may be found.

Paræsthesia often occurs. Schech observes that the affection, when independent of disease of the mucous membrane, is most frequently associated with hysteria and hypochondriasis, or with a fear of diphtheria or syphilis. Those individuals are most prone to it whose occupation demands excessive use of the vocal organs, as also are chlorotic or anæmic persons, women who suffer from gastric or uterine disease, and those whose temperament is excitable; more rarely it is a symptom of disease of the brain, or of bulbar paralysis.

Of the motor disturbances from which the velum may suffer, spasm is the more unusual. It is almost always associated with a similar condition of the pharynx, and is found associated with the same disorders as those which cause it in the latter region.

Paralysis of the velum is a common condition, and one of much importance. It may be due to central causes, such as acute, chronic, and degenerative diseases of the brain; to diphtheria; to local diseases; or, finally, it may be associated with facial paralysis. The paralysis may be either unilateral or bilateral, partial or complete. When it is unilateral the velum and uvula are drawn toward the unaffected side, the faucial arch on the affected side is wider, and that of the sound side is narrower than normal. During phonation there is distinct distortion toward the healthy side. In bilateral paralysis the uvula hangs loosely in the pharynx, showing no sign of voluntary motion, and flapping back and forth with the acts of respiration. During phonation, in partial paralysis, a slight upward movement of the soft palate may be noticed, while, when the paralysis is complete, it remains immovable.

Besides the causes mentioned, there are several influences under which paretic conditions of the velum may occur. Thus, it is not uncommon to find this organ more or less paralyzed after severe acute affections of the pharynx other than diphtheria, and while the presence of such paralysis, after what appeared to have been a simple follicular tonsillitis, may cause the accuracy of the diagnosis to be held in question and suggest the presence of diphtheria, there are so many other disorders, evidently not diphtheritic, by which it may be brought about that the possibility of its occurrence from simple causes is beyond doubt.

Not only may paresis be found after acute affections of the throat and nasopharynx, but, as is more common, it may be present in chronic conditions, as, for instance, chronic pharyngeal catarrh, chronic hypertrophy of the tonsils, and hypertrophy of the adenoid tissue at the pharyngeal vault. It is found in cases of chronic nasal catarrh, and associated with posterior hypertrophy of the inferior turbinated bodies. It may also occur as an accompaniment of an elongated uvula.

The results of this condition are generally evident, both to the patient and to the observer, and it is probable that the defects of speech generally present in, and attributed to, adenoid hypertrophy at the vault, are due rather to the attendant paresis of the soft palate than to the mechanical obstruction of the pharynx.

The treatment of neuroses of the soft palate must be conducted in accordance with the exciting cause present in a given case. This must be demonstrated, and, if possible, removed. Catarrhal conditions must be treated, hypertrophied masses of adenoid tissue must be removed, and the various systemic disorders with which it may be associated properly dealt with.

Locally, direct therapeutic measures are required, the most important thing being to restore tone to the enfeebled muscular structures. To this end the faradic current is valuable, the negative pole being applied to the affected part, or outside, along the angle of the jaw. Systematic exercise of the velum is also beneficial, and may be secured by such gymnastic exercises as frequent gargling, the singing of high notes, or, better still, blowing through a small tube. In the case of children this may be accomplished by allowing the patient to practise daily at blowing soap bubbles. *D. Bryson Delavan.*

VACCINATION is defined as "Inoculation with vaccine, or the virus of cowpox, as a preventive of smallpox; in an extended sense, inoculation with the virus of any specific disease. . . . It consists in the introduction under the skin, or application to an abraded surface,

usually on the upper arm or thigh, of a minute quantity of vaccine." —*Century Dictionary.*

"Inoculation with the attenuated or modified virus of a disease, to produce a mild form of it, and so prevent a virulent attack; specifically, and originally, inoculation with cowpox as a preventive of smallpox; performed by introducing vaccine through a puncture of the skin, or an abraded surface."—*The Standard Dictionary.*

For legal purposes, it should be added that the term "vaccination" not only implies the application or introduction of vaccine to or into the body, but its *successful* application or introduction.

In this article the term will be employed only in its limited sense, as applied to the specific disease vaccinia or cowpox.

The *object* of vaccination is, ultimately, protection against smallpox. As a means to the same end, it is also largely employed for the purpose of propagation, continuance, and multiplication of the virus of vaccinia.

History.—To Edward Jenner, an English surgeon of the eighteenth century, must be accorded the honor of introducing and establishing the practice of vaccination as a protective measure against smallpox. The history of vaccination is like that of many other important discoveries. It had a traditional existence from an earlier period, and had undoubtedly been practised to a limited degree in other countries. Von Humboldt states that it had been known and practised from an early period among the Mexicans. Sülzer in 1713, and Sutton and Fewster in 1765, called attention to the properties of vaccine.[1] But no one had given to the subject careful observation and study until Jenner, then a surgeon's apprentice living at Sodbury, near Bristol, noticed that people who acquired cowpox by milking cows affected with that disease acquired an immunity from smallpox. From the time of his first observation, in 1768, to the date of his announcement of the result of his researches to the world, a period of thirty years elapsed, during which time he had patiently and carefully investigated the subject both by observation and by experiment. Dr. H. A. Martin says of him: "He was a truly great and philosophic man, worthy to be, as he was, the chosen pupil and life-long friend of John Hunter. If ever a discovery was announced to the world with due deliberation, it was that of vaccination. We have evidence that for at least thirty years, during which he encountered many perplexing and discouraging obstacles, and one by one mastered and overcame them, this mighty matter occupied the brain of Jenner before he published 'An Inquiry into the Causes and Effects of the *Variolæ Vaccinæ*, a Disease discovered in some of the Western Counties of England, particularly Gloucestershire, and known by the name of Cowpox.' It was ten years after the discovery first engaged his attention that, in the year 1780, timidly, and under the seal of confidence, he revealed to his bosom friend, Gardner, his mighty hopes for the great good of his fellow-creatures. . . . Such was the slow, careful, almost painful deliberation and completeness with which the mind of Jenner moved to its great goal."[2]

Jenner made his first vaccination upon the human subject in 1796, published the results of his inquiries in 1798, and established the first public institution for the performance of vaccination in 1799. In 1800 the practice was introduced into Germany, France, and the United States.

To Dr. Benj. Waterhouse, of Cambridge, Mass., must be credited the honor of introducing vaccination into New England in 1800, and to President Thomas Jefferson that of introducing it into the Southern States a few months later. It was also introduced into France in May, 1800, by Duke de Rouchefoucault, his efforts being seconded by Napoleon, and especially by his brother Lucien Bonaparte, who was then Minister of the Interior. Dr. Woodville also came over from London to insure the success of the movement.

The following were the principal points which Jenner had established by his inquiries:

1. That the vaccine disease casually communicated to man has the power of rendering him insusceptible to smallpox.

2. That the specific cowpox alone, and not other eruptions affecting the cow which might be confounded with it, has this protective power.

3. That the cowpox may be communicated at will from the cow to man, by the hand of the surgeon, whenever the requisite opportunity exists; and

4. That the cowpox, once engrafted on the human subject, may be continued from individual to individual by successive transmissions, conferring on each the same immunity against smallpox as was produced in the one first infected directly from the cow.

The practical usefulness of this great discovery lies in the possibility of transmitting vaccinia from one human being to another, or, as is largely practised at the present time, from the cow to the human species.

Phenomena of Vaccinia in the Cow.—Vaccinia in the cow is an eruptive vesicular disease, the eruption being usually limited to the udder and the teats. It may occur in single cases, either in an animal kept alone, or in a single animal of a herd, or it may attack a whole herd, or a part only.

It is confined almost exclusively to milch-cows. Ceeley's earlier observations supported this statement; but in a later paper he reports a single case of primary infection in an animal not giving milk. The earlier stages of the disease are so mild as rarely to attract attention, and hence are rarely seen by the expert at this period, except in herds in which the disease attacks a considerable number. After its first appearance in a herd, it is readily conveyed from one animal to another by the milker's hands, unless the greatest care is taken to prevent infection.

Distribution.—Vaccinia has been met with and described in all parts of the world where the cow exists. In Great Britain, France, Germany, Holland, Italy, Bengal, South America, Mexico, New England, and other States of the Union, cases have been reported and described, and in not a few of these the genuine character of the disease was proven by experiment. It was found in epidemic form at Valladolid and at Atlisco, in Mexico (near Puebla), in 1803. Genuine cowpox was also observed in Würtemberg, on 69 different occasions, between 1827 and 1837, and was transferred successfully to the human subject in at least 170 out of 210 trials (Hering: "Ueber Kuhpocken an Kühen"). Seaton says of its prevalence: "After the first ardor of search had relaxed, there were for many years but few recorded instances of the disease being found, and it was believed to have become much rarer, in great measure, no doubt, because it was less sought for. There can be no doubt that much more would be found than really is found, if it were only looked for." Other noted cases were those which were observed at Passy (1836), at Esneux (1868), at Rouen, at Dijon, at Stuttgart, at Beaugency (1866), at St. Mandé, and at Cerons (1884).

A very careful report of an epidemic of vaccinia is presented in the Eighteenth Report of the Local Government Board of England (supplement containing the report of the medical officer for 1888).

Not far from the foregoing case, at Cricklade, in the neighboring county of Wiltshire, other cases of cowpox were discovered in the autumn of 1887, of which an account is given in the second volume of Crookshank's "Vaccination: Its History and Pathology."[3] This region also is not far from the district in which Jenner made his early observations. In a herd of one hundred and twenty cows here, all were attacked except a dozen, which proved refractory.

Occurrence of Natural Kinepox in the United States.—Kinepox is not of unusually rare occurrence, as some have believed. It has been observed on various occasions, and at various places, in the United States, and reported as follows:

1. Dr. John Yale, of Ware, Mass., reports having observed it in 1844, at Torringford, Conn., and in 1855 at

Ware; in the latter case confirming its character by testing it upon the human species, and also by continuing its use upon calves. (Transactions of the American Medical Association, 1872, p. 216.)

2. Dr. Currier observed it at Lexington, Mass., in 1850, and tested it by insertion upon infants.

3. Dr. E. Cutter observed it upon several occasions, as stated in his report of 1872.

4. Dr. H. Darlington observed it and reported upon it as occurring at Concordville, Pa., in 1872.

5. Drs. McMillan and Trask observed it in Marion County, Cal., in 1871, and confirmed its character by experiment.

6. Dr. Jonathan Brown observed it in Wilmington, Mass., in 1867, and tested it by experiment.

7. Dr. H. A. Martin reported a case as observed by him at Cohasset.

8. Cases were reported at Reading, Pa., in 1872.

9. The writer has also visited and inspected at least twenty cases which occurred at seven different dairies or farms in Middlesex and Essex Counties, in Massachusetts, in 1872, 1873, 1881, and 1882. These all occurred during the prevalence of the two smallpox epidemics of those years. They were examined at different stages of the disease, and were found to have the characteristic appearances described by the earlier investigators upon the same subject. At one large dairy farm, where about ninety cows were kept, several cases were seen in different stages, and the disease was prevented from spreading only by isolation and absolute separation from the milkers who milked the remainder of the herd.

Dr. Petry, a noted veterinarian, of Esneux, says: "This disease is much more frequent than is commonly believed. Cowpox may be found in every place, in every land, and in every season of the year; but oftener, it is true, in spring, and in summer at the time of calving." ("Quelques réflexions sur la prétendue rareté du cow pox chez la vache," par M. Petry, M. V. à Esneux. *Annales de la Soc. Méd. Chirurg. de Liége*, 17, 1878.)

Other cases have been observed in recent years in the same vale of Gloucester in which Jenner made his original researches, and also in many other English localities. The writer also has examined dairies at which animals were pointed out by the owners as having had cowpox in previous years. In several of these, by way of experiment, the animals were vaccinated by an expert vaccinator, and in such cases the vaccination invariably proved unsuccessful—a point which may be adduced in support of the genuineness of the disease as at first observed.

In a case observed by the writer at Saugus, in the winter of 1881-82, a lad, twelve years of age, presented the characteristic appearances of infection upon the grasping surface of the index finger and thumb. When first observed most of the vesicles had been broken by the use of the hand in milking. The herd consisted of thirteen animals, but one only of which was found to be suffering with cowpox.

The disease, though not by any means of rare occurrence, is evidently not so common as it was in the eighteenth century, and Dr. Seaton reasonably adduces as causes of its comparative rarity the more common practice of vaccination, whereby milkers do not become susceptible of infection, and, as a consequence, are not the conveyers of such infection from one animal to another; and secondly, the more limited diffusion of variola.

The term "spontaneous" formerly applied to such cases should be abandoned as entirely opposed to all observations as well as modern medical belief as to the natural history of infectious diseases.

Incubation.—The incubative period is probably about three or four days, prolonged occasionally to seven or eight days (Ceeley). At first there are heat, swelling, and tenderness of the parts affected, hard papules are developed of the size of a small pea, especially at the base of the teats, at the junction with the udder. The signs of constitutional disturbances at this time are but slight. In thin-skinned animals the disease may be found, by careful observation, when accidentally transmitted, as early as the fifth day. The papules increase daily, and in three or four days from their first appearance become distinctly vesicular, and have a more or less central depression.

The change from the papular to the vesicular stage is indicated by the appearance of a dull yellowish point at the apex of the prominence; the circumference then increases in substance and extent, and the centre becomes wider and deeper, till at last the flattened vesicle with depressed centre is formed. It increases in size until, in three or four days more, its full development is reached. Their number and size vary. The amount of eruption varies with the severity of the disease. With animals having loose, fleshy, hairless udders, and long, thin-skinned teats, the eruption is ordinarily copious. The shape of the lesions is usually determined by their position, being for the most part circular at the base or neck of the teats, and oval on the body of the teats. Their color varies with the stage of the disease and the color of the skin. When completely formed the vesicle is often from 15 to 20 mm. in diameter, and has a solid, tense, shining margin of a glistening white or silvery hue, and a bluish or slate-colored centre. It contains a viscid, clear lymph, which is at this period quite scanty. Around the base a narrow, rose-colored areola begins to spread with a circumscribed induration. The color of the areola varies with that of the skin. The disease reaches its crisis about the tenth or eleventh day. The lymph becomes more copious, the vesicle becomes more globular in form, and if it is broken, the lymph flows freely. At first it is of a light amber color, and then becomes turbid and opaque. Incrustation now begins at the centre and advances steadily, the crusts attaining their largest size by the thirteenth or fourteenth day. They are of a dark-brown color, and adhere more or less firmly to the skin, the areola and the induration gradually subsiding. The crusts continue to dry and to diminish in size, and become loose and fall off about from the twentieth to the twenty-third day. The cicatrices left are shallow, smooth, and of a pale-rose or whitish hue.

These are the appearances of undisturbed vaccinia in the cow, and they are rarely seen in their perfect form, since the handling of the teats by the milkers injures the vesicles, rupturing the cuticle, and allowing the serum to exude. Raw surfaces and dark crusts are often seen coalescing, and becoming rapidly detached by rough usage. The tender teats, with their raw surfaces, bleed, and finally heal, leaving cicatrices of varying size.

Constitutional Symptoms.—These are usually slight. The appetite of the animal appears to be affected but little. The secretion of milk may be slightly diminished, and the amount actually obtained may be much lessened in consequence of the annoyance to the milkers and trouble in milking.

There is no evidence that the quality of the milk is in the least modified. Both in the casual form of vaccinia and in that which is artificially produced, animals have been known to give milk uninterruptedly through the course of the infection, and such milk has been in constant use, without perceptible detriment to consumers.

Spurious Eruptions.—The cow is liable to other eruptive diseases which may be mistaken for vaccinia. Ceeley mentions three varieties, under the names of the yellow, the black, and the white or blister-pock, the latter being quite contagious. More recently other eruptions of a contagious nature have been observed and described, especially that which is associated with scarlatina, and which appears to have given rise to that disease in human beings, either through the medium of the milk or otherwise ("Local Government Board Report," 1882. Inquiries by Mr. Power and Dr. Klein, p. 63).

The Relation of Vaccinia to Variola.—*The Unity or Duality of the Two Diseases.*—Seaton states that the common origin of the cowpox, horsepox, and smallpox has been established by conclusive experiments, and adduces the experiments of Gassner, of Günsburg, in 1801, who inoculated eleven cows with smallpox virus, in one of which vesicles appeared, from which several children

were successfully vaccinated, the ordinary phenomena of vaccination ensuing (Henke's *Zeitschrift, Ergänzungs.*, p. 57).

In 1865 a commission at Lyons published the following conclusions concerning the relation of these diseases to each other:

1. Cowpox and smallpox can be inoculated in bovine and equine animals; the first energetically, the second feebly.

2. Whatever may be their successive transmissions, direct or crossed, these two diseases breed true on every soil.

3. The protection from one by the other is assured in every case.

Some interesting experiments have been made by Haccius and Eternod, of Geneva, which tend to confirm those already published by Fischer in the *München. med. Wochenschrift*, and make the identity of variola and vaccinia more than probable. The conclusions at which Thiele, Ceeley, Voigt, and Depaul arrived many years ago, namely, that cowpox is a modified form of smallpox, attenuated by its passage through the organism of an animal, were disputed by the Lyons commission, which adduced seemingly unimpeachable experiments of their own, contradictory to the observations of the earlier experimenters.

Haccius and his colleague, following the operative method of Fischer, claim that they have succeeded in imparting smallpox to animals, and in transmitting it through several generations, the disease finally manifesting itself in a mild form not distinguishable from true cowpox, and like it, conferring immunity from variola.

In one of these series of experiments, Haccius and his colleague succeeded in transmitting the smallpox virus from heifer to heifer to the fourteenth generation; and side by side with a set of similar observations where vaccine virus was used, they had a series under observation where the heifers were inoculated with virus from a case of confluent smallpox. Lymph from "the fourth generation" has given the results of ordinary vaccine when used for purposes of vaccination.

Their conclusions were as follows:

1. Variola is inoculable *with certainty* on the bovine species when the operative method is such as it should be, and the virus is collected at the opportune moment.

2. The inoculation of the heifer with smallpox constitutes a valuable source for new reinforcements of animal vaccine. This may be of great practical benefit, not only to the vaccinal institutes of Europe, but also to tropical countries, where smallpox is endemic, and where the generations of vaccine tend rapidly to deteriorate.

3. Smallpox inoculated in the heifer becomes transformed into vaccine in the course of several generations, by transmission through the animal. *Duality is thus disproved.*

4. Our practical conclusions confirm the views enunciated by Depaul, in 1863, to the Academy of Medicine of Paris.

Following these experiments Chauveau was led by a similar mode of investigation to very different conclusions.

His paper ("Sur la transformation des virus à propos des relations qui existent entre la vaccine et la variole") was presented at the sessions of the Academy of Medicine of October 20th and 27th, 1891. His conclusions are as follows: (1) Vaccine virus never gives smallpox to man. (2) Variolic virus never gives vaccine to the cow or horse. (3) Vaccine is not even *attenuated smallpox*, and cannot be compared to the benign anthracoid infection which is communicated to animals by inoculation with *attenuated anthracoid virus*. (4) If vaccine is a derivative of smallpox it is by reason of a *radical transformation* of the variolic virus, a transformation thus far unattainable by experimenters. (5) These last propositions lead to another more general proposition, which is this: the *attenuation* of virus is not a physical process which can be identified with the *transformation* of virus. The weight of scientific opinion to-day, however, is decidedly against these conclusions of Chauveau.

Satisfactory experiments of this kind are difficult of performance, for no experimentation on animals can be regarded as complete the results of which have not been checked by inoculations practised on the human subject. Now, Haccius and Eternod did not try their lymph—rendered vaccinal, as they believed, by several removes—on the unvaccinated child, nor did Chauveau make any such trials (*Boston Medical and Surgical Journal*, 1891).

On the other hand, it appears that the experiment has been tried upon unvaccinated children in Calcutta, as detailed by the experimenter, Dr. W. J. Simpson, medical officer of health of Calcutta, at a meeting of the Calcutta Medical Society, April 13th, 1892.

Dr. Simpson comments upon Chauveau's experiments as follows: "Seventeen animals were inoculated by that commission with lymph from virulent cases of smallpox, and some small papules were obtained, the secretions from which, when inoculated into other cows, gave rise to papules of an insignificant kind, but which when inoculated into children gave rise to smallpox. On this slender foundation the theory has been based, and is very forcibly put forward, that smallpox in man produces a real smallpox in the cow totally differing in every respect from cowpox.

"To those who have studied the subject these experiments are by no means conclusive. They only show that Chauveau with his coadjutors failed to inoculate the cows successfully, and that the papules raised were rather due to the irritation of the points of insertion by the smallpox lymph, and that the serous matter taken out of these papules was the smallpox lymph itself, which had remained in them unchanged; and under these conditions it was not surprising that smallpox was produced in the children inoculated with this virus.

"Nothing further was attempted in the way of experiment until Dr. Klein, in 1879, inoculated thirty-three cows with smallpox lymph, but failed to raise any vesicles on the cows. Papules appeared in some of the cows at the seat of inoculation, but these were not considered to have turned the experiments into a success, and no serum was taken from these papules and inoculated into children. If such a procedure had met with favor, there would probably, as in Chauveau's cases, have been an after-history of smallpox in the children inoculated.

"Dr. Klein's failure served to accentuate the theory based on Chauveau's disaster, and both failure and disaster were employed as a basis on which arguments were founded against the pathological identity of smallpox and cowpox. So confident have the supporters of this view since become, that strong doubts have been expressed by them as to the genuineness of the experiments performed by previous observers. A favorite argument appears to be that what was accomplished in the earlier part of the century cannot be done now, and therefore the experiments are not altogether to be trusted. The reason of this is not far to seek. All the conditions under which the cow may be successfully inoculated are not known, and hence it is not every cow that can be inoculated with success. This entails on the investigator much expense, the exercise of a great deal of trouble and patience, and of course it is much easier to read up the subject as Professor Crookshank has done, and side with the view for which you may have the greater predilection, than thoroughly to investigate the subject, not being satisfied with dubious results.

"Apart from the controversial question, it has for a long time been a matter of thought with me as to whether there is any relationship between cowpox, horsepox, sheeppox, and smallpox; whether these four diseases have for their cause a common origin which may be designated by the letter x, this common origin having not yet been discovered; or whether horsepox, cowpox, and sheeppox, or any of them, are descendants of smallpox; or thirdly, whether smallpox may be looked upon in the light of a parasitic disease which comes to its full development in man, enters some animal as the cow, losing that which gives it its infectious properties, and then in some other animal, unknown as yet in the soil, regains

that element which it had lost in the cow, and which once more renders it infectious.

"I am inclined to think that it is in this latter direction that investigation will ultimately succeed in discovering the cause of the periodicity of smallpox.

"Vaccine and chickenpox have always seemed to be two elements of smallpox which have become separated in some unknown way, the vaccine retaining the peculiar qualities belonging to the smallpox which affects the body in such a manner as to render it immune from a second attack, while the chickenpox has none of these qualities but has retained the infectious element. If this were true, it might seem to be easily proved by experiment. I have tried the experiment by mixing the two viruses, but without success. There is a difference, however, between mixing and combining, and it is possible that the conditions which affect this have to be found in some other less simple way.

"It is for the reasons stated, and for some others which I need not mention here, that I have been engaged for years, as opportunity arose, in experimenting with smallpox on animals.

"When in Aberdeen I used to search the farms in the country for cowpox, and not without success. I have inoculated cows, horses, sheep, pigs, goats, fowls, monkeys, and dogs with smallpox virus to ascertain the result, and in these experiments I have succeeded incidentally; for it was not the primary object for which I began the investigation, in converting smallpox into ordinary vaccine by passing the virus from an unprotected smallpox patient through the cow.

"In December, 1884, I first succeeded in raising a vesicle in a cow after inoculation with smallpox virus. The lymph was transferred to a ewe lamb, and raised a vesicle in every appearance similar to a vaccine vesicle. This lymph was taken and introduced into a young pig six weeks old, and here it was lost.

"In November, 1885, with smallpox lymph from an unvaccinated patient, I inoculated a cow with fifth-day lymph, and a ewe with eighth-day lymph from the same patient. Both presented vesicles on the seventh day, the lymph of which I sent to London to be used by Dr. Cory, the director of the Animal Vaccine Institute in London. This calf lymph, which Dr. Cory passed through a second calf before using on children, was the starting of a new stock of vaccine at the Institute.

"Between November 21st, 1885, and May 6th, 1886, 1,247 children had been vaccinated with this lymph, and gave 98.4 per cent. insertions of success."

These experiments of Dr. Simpson were also confirmed by similar experiments made by Dr. W. G. King, of Madras, and by Dr. T. W. Hime, of Bradford, England (*Practitioner*, vol. xlix., 1892; *Brit. Med. Jour*, July, 1892).

The Phenomena of Vaccinia in Man.—Vaccinia is communicable to man only by inoculation, and may be communicated with equal certainty from the cow or from other human beings.

When fresh vaccine lymph is introduced into the unvaccinated human subject, either by puncture or by abrasion of the skin, local effects are not usually noticeable within the first forty-eight hours. The period of incubation is brief, and if the vaccination is successful, at about the end of the second day a slight redness and swelling are observed at the seat of insertion. On the third or fourth day a little vesicle appears at the summit of the papule, filled with a clear liquid, which gradually grows larger and larger. As the size of the efflorescence increases, an umbilication appears, similar to that of the genuine variola pustule, which corresponds to the shape of the original wound of insertion; an insertion by simple puncture producing a circular vesicle, and an insertion by a longitudinal incision producing an oval vesicle. The vesicle attains its largest size about the seventh or eighth day, when it contains a clear liquid, which, if the vesicle is punctured, will ooze out upon the surface sparingly. The construction of the vesicle is cellular, like that of the pustule of variola. After the eighth day, and sometimes a few hours earlier, a ring of inflammation called the areola begins to form about the base, and the vesicle and areola together continue for the next two days to spread. The areola is circular, and when fully developed has a diameter of 1–3 in. (2½–7 cm.). It is often attended with considerable hardness and swelling of the subjacent tissues. The establishment of the areola demands attention as the evidence that the specific effects of vaccinia have been produced. If several insertions have been made near each other, the areolæ coalesce.

After the tenth day the areola begins to fade, the vesicle begins to dry in the centre, the lymph remaining in it becomes opaque, the pearly colored pustule becomes yellowish, while at the centre, at the location of the original insertion of the virus, a crust has begun to form. By the fourteenth day the crust has become dry and hard, and gradually assumes a darker hue, and usually falls off from the twentieth to the twenty-fifth day, leaving a cicatrix, commonly permanent, which is usually circular, slightly depressed, foveated, or indented with minute pits, and sometimes radiated. (Plate LVIII.)

There are also constitutional symptoms more or less severe, in proportion to the intensity of the local symptoms. There are fever, restlessness, derangement of the digestive organs, and occasionally swelling of the axillary glands. The constitutional symptoms are usually most severe at or a little before the time when the areola has reached its fullest development. Infants usually suffer less than older children, and these less than adults. In adults the course of primary vaccinia is apt to be more retarded than it is in infants, the areola is often more diffuse, and the swelling of the axillary glands more common.

All of these phenomena may be modified by acceleration, by retardation, or by irregularity of development.

1. The most common form of modification is a slight *delay* in the development of the usual symptoms, of one or more days, so that by the ninth day the vesicle has arrived at the usual condition seen upon the seventh or eighth day. Seaton mentions cases in which a week's delay was observed, and after success had been given up; and Bousquet mentions a case in which a dormant vaccination was revived at the end of three weeks. This delay is sometimes due to the incubation of other diseases. If the phenomena follow a regular course, this retardation does not necessarily imply an interference with the protective power of the vaccination.

2. *Acceleration* of the phenomena of vaccination is to be regarded with more suspicion than retardation. If the acceleration amounts to not more than one day in advance of the usual appearances, and the vesicle and the consequent areola assume the typical form and color, the protective value of the vaccination is not necessarily impaired.

3. Vaccination may present *irregular forms*. The formation of the vesicle may be accompanied by considerable itching and irritation. Its shape may be acuminated or conoidal, and without the central depression, and the fluid contents may not be a clear serum, but a cloudy liquid. The areola may be formed early and may be irregular in shape, arriving at its height on the fifth or sixth day. A crust may form and fall off as early as the tenth or twelfth day. The local effect may have been still more accelerated, and a thin scale formed which is readily detached.

Other irregular forms may be seen, none of which should be depended upon as protective against smallpox, nor should virus be taken from them for the purpose of vaccinating others. Such irregular conditions are doubtless due, either to the use of vaccine lymph which is not sufficiently recent, and has consequently lost much of its active infective power, or it may have been inserted in a subject whose health is bad; so that the results of the vaccination may appear uniform from virus employed under the first of these conditions, but not under the second.

Mechanical irritation, such as may be produced by a coarse woollen sleeve, may occasionally interfere with

the usual phenomena of the vesicle, by causing its rupture or irregular appearance, and these phenomena may be aggravated if the garment is colored with poisonous dyes. It is a matter of necessity that proper instructions should be given to parents or guardians for the protection of the vesicles, that they may remain uninjured.

With reference to the general question of irregular phenomena, it may be taken as a rule of practice that *any vaccination which presents a deviation from the perfect character of the vesicle, and the regular development of the areola, should not be relied upon as protective against small-pox, nor should lymph be taken from such a vesicle for further use in vaccination.*

Effect of Climate.—In temperate climates the utmost effect of season, either hot or cold, is only to accelerate or to retard (and that exceptionally and seldom beyond a few hours) the usual course of vaccination. According to the best authorities, the excessive heat and moisture of certain seasons in the tropics interfere considerably with the regular progress of vaccination. In India vaccination is less successful after the advent of the hot season, and it is peculiarly so in the rainy season in Bengal, "so much so that vaccination must necessarily be suspended for a time" (Report of Smallpox Commissioners in 1850. Indian Government).

In other parts of India these precautions are not found to be necessary. In the cooler parts of India vaccination may be performed at any time, but in the hotter portions the best season for vaccination is from October to March.

Revaccination.—In some people the regular phenomena of vaccination can be produced but once in a life-time. A subsequent introduction of vaccine virus either fails to produce any effect whatever, or it produces a modified effect, like that of spurious vaccination. Revaccination is desirable in all cases of imperfect vaccination, and in all persons at the end of ten or twelve years after a primary vaccination in infancy; and also, in case of immediate exposure to smallpox, it is advisable in those who have not been vaccinated within five years. It should be understood, however, that the human body is not subject to mathematical rules and limitations, and hence, like many other principles of medicine, no precise limit of safety can be stated. The writer has vaccinated persons successfully, who had been successfully vaccinated within a year previous, and has also found many in whom vaccination with fresh lymph was unsuccessful after twenty years or more from the date of a previous vaccination.

Under no circumstances should the lymph from a vesicle of revaccination be employed for further use in vaccination.

As revaccination is a preventive measure, like vaccination, it should not be left until the occurrence of an epidemic. In the United States, where public vaccination is imperfectly carried out, it is a common custom to await the outbreak of smallpox, at which time it is more likely to be done with less care, and in consequence of individual fear rather than according to the discretion of the physician.

The immediate results of revaccination may be either the development of a typical umbilicated vaccine vesicle or of a modified vesicle, or entire failure.

The claim once made by the earlier vaccinators, that a singe primary vaccination was absolutely protective for life against smallpox, is no longer tenable, since experience in severe epidemics in large communities has shown abundant proof to the contrary. After several years had elapsed from the date of the introduction of vaccination, it was observed that cases of smallpox occasionally occurred in the persons of those who had been vaccinated; such cases, however, being of a mild type and rarely fatal. It was therefore urged that the protective power of vaccination was only temporary, gradually becoming less as the individual grows older. By some, the occurrence of such cases was attributed to an improper or an inefficient performance of the primary vaccination. Early observations in support of such belief were made in Copenhagen, and also in London.

In every community a certain proportion of the inhabitants will take smallpox, if they rely merely on the protection which is afforded by a single vaccination performed in early life.

The great standing armies of Europe afford conclusive evidence as to the need of revaccination. It was introduced into the Russian army in 1831, and for the ensuing years from 1831 to 1857, the number of revaccinations was 733,332, of which number 391,574, or 56 per cent., were successful, and 228,848, or 31 per cent., were unsuccessful; the remainder were imperfect.

Seaton lays down the rule that *carelessness in primary vaccination should not be excused on the ground that revaccination will supply its defects.* "It has too often happened," he says, "that vaccination has taken, but has taken badly; either at once or at some not distant period it has been repeated, and has perhaps been performed a third time, but ineffectually (for it will constantly happen that spurious vaccination will prevent subsequent vaccination from taking effect properly); then no more is thought about it, or the child is declared 'insusceptible'; it grows up, gets smallpox, and very likely dies. Take it at its best, an originally imperfect or incomplete vaccination is a very great misfortune."

Age at which Revaccination Should be Performed.—There are circumstances which would call for its performance in childhood, as when the primary vaccination is found to be spurious, imperfect, or irregular in character. If, however, the child's health appears to be such as to account for the irregularities and imperfections, the vaccination should be deferred until its health is corrected. Especially should children having imperfect cicatrices be revaccinated, if there is danger of immediate exposure to infection from smallpox.

Revaccination should be performed with the same care as primary vaccination and always, when possible, with fresh lymph.

It should not be left to periods when smallpox becomes epidemic, and its performance upon persons arriving at a certain age, say twelve years, should be as systematically carried out as in the primary vaccination of infants.

From the results observed as to the performance of revaccination in the armies of Great Britain and of Würtemberg in 1831, 1835, and 1861, it was concluded that the local results obtained by the revaccination of any individual gave absolutely no information whatever as to the constitutional condition in which the revaccinated person was with regard to his liability to contract smallpox.

Dr. R. Gerstäcker, in a paper entitled "The Hygienic Significance of Revaccination,"[4] gives some valuable data compiled from the reports of the Imperial Board of Health, and also from the report of the Vaccination Commission. From their tables it appears that the mortality from smallpox in Prussia, formerly differing but little from that of other countries, has fallen to a minimum under the operations of the vaccination law, so that smallpox may now be regarded as having disappeared, except in some frontier districts; while Austria, with her defective regulations as to vaccination, and still more so as to revaccination, suffers severely from smallpox. Dr. Gerstäcker presents the following table as to the mortality from smallpox in London and in Berlin, with the comment that, while London enforces vaccination of the children, it has not enforced revaccination. He attributes the difference in the relative mortality from smallpox in the two cities to these facts.

Deaths from Smallpox, per 100,000 Inhabitants.

	1875.	1876.	1877.	1878.	1879.	1880.	1881.	1882.	1883.
In London	1.3	20.8	71.0	38.8	12.1	12.5	61.9	11.1	3.4
In Berlin	5.2	1.8	.4	.8	.7	.8	4.7	.4	.3

Dr. Gerstäcker further agrees with the conclusions of the earlier observers, as to the immunity against smallpox produced by primary vaccination in childhood being of limited duration, and as to the possibility of renewing

EXPLANATION OF
PLATE LVIII.

EXPLANATION OF PLATE LVIII.

The vaccinations shown in this plate are those of three infants, from four to ten months old, at different stages of vaccination. Figs. 2 and 3 are from the same child on different days. Four insertions were made in each case, according to the usual practice of official English vaccinators. These insertions are usually made by light parallel scratches, two or more in number, and about 3–5 mm. in length.

Fig. 1 presents the appearance on the fifth day. The linear depressions in the vesicles indicate the location of the insertions of lymph. A faint flush is appearing around each vesicle.

Fig. 2 shows the appearance on the eighth day.

Fig. 3 presents the appearance at the end of twelve days. In this and in Fig. 2 some supplementary vesicles are shown, a matter of common occurrence. The course of development has been more than usually rapid in this case from the eighth to the twelfth day, desquamation being active around the vesicles and the brownish coloration of crusts appearing.

Fig. 4.—Appearance on sixteenth day. Shows typically the usual method of desiccation of the vesicle.

FIG. 1. SIXTH DAY.

FIG. 2. EIGHTH DAY.

FIG. 3. TWELFTH DAY.

FIG. 4. FIFTEENTH DAY.

PRIMARY VACCINATION.

Reduced from coloured illustrations in Pathological Society's Transactions, Vol. [illegible].

its influence by repetition. Revaccination, therefore, as he expresses it, forms an essential part of the measures of prevention against smallpox, and its hygienic importance extends not only to the individual, but also to society, the relative immunity of which is warranted only by the immunity of the individual from smallpox. He reckons the protective period of primary vaccination at an average of ten years, and therefore believes the revaccination of school children in the later years of school life to be essential to complete immunity.

Dr. Seaton sums up the purposes of revaccination as follows:

1. To repair whatever was irregular in the course of a primary vaccination.

2. To supply what was imperfect in the amount of infection, in cases in which the course of the disease was regular.

3. To extinguish the susceptibility to smallpox which may remain, or may rearise, in an indeterminate number of persons whose primary vaccinations may have been complete as well as regular ("Seaton's Handbook," p. 300).

Autovaccination.—By this term is meant the reinsertion of fresh vaccine lymph upon the same person from whom it is taken, either by the vaccinated person himself or by some other person, and also either intentionally or by accident.

Vaccinization.—In a paper published by the Belgian Academy of Medicine, entitled "La Pratique de la Vaccine; ce qu'elle est, ce qu'elle devrait être" (1885), the author, Dr. Titeca, concludes that the principles of vaccination should be raised to the state of an axiom; in other words, that it may be made perfectly protective. Dr. Warlomont has expressed a similar belief.[5] They have crystallized this belief under the name of the school of vaccinization (école vaccinisatrice), wherein they are in accord with the views of many others, both in America and in Europe.

The author concludes that vaccination is in many cases *nothing but a deceptive operation performed with a hypothetic virus.*

The following questions are also discussed by the same author:

1. *No vesicle follows a given vaccination.* We are not therefore to infer that the subject is wholly insusceptible and abandon the attempt to secure a successful result.

2. *One or more vesicles are developed.* The subject, therefore, *ipso facto*, should not be regarded as having acquired immunity from smallpox. An old regulation of the German army required twenty insertions, ten in each arm.

In Holland, a modified vaccination has been practised for a long time, ten insertions being made upon each subject, and the results classified in accordance with the number of good resulting vesicles, certificates being given to such as have more than five good vesicles. All others are submitted to a supplementary, or an autovaccination.

Dr. Titeca gives the results of twenty-three primary vaccinations of children of various ages from three months to five years: twelve boys and eleven girls, showing the possibility of exhausting the susceptibility of the subject by means of repeated vaccinations.

From a general review of the subject the author concludes that vaccination, to be perfectly protective, should be practised under the following conditions:

1. The employment of a vaccine virus which has lost none of its vitality.

2. The number of inoculations should be in accordance with the individual vaccinal receptivity, even to the extent of the exhaustion of that condition.

The first of these conditions is fulfilled by the use of living (*vivant*) vaccine, collected at the time of the operation; the second by the operation to which Dr. Warlomont gives the name of vaccinization.

Every vaccination made in default of these conditions is deceptive, and to such faulty methods the antivaccination school owes its existence. Its faults and grievances will cease when the school of vaccinization is recognized.

The author recommends the following practice:

1. Vaccinization of infants within six months of birth.

2. Revaccinization every ten years, when no epidemic is prevailing, and general revaccinization in time of epidemic.

Insusceptibility.—It is quite probable that under the most favorable circumstances for vaccination (absolutely fresh lymph in each instance), insusceptibility in primary cases does not exist.

Dr. Robertson says, in the twenty-fifth "Report of the Registrar-General of Scotland": "Constitutional insusceptibility, as expressed in the returns, is virtually a confession from an operator that he has made three unsuccessful attempts to vaccinate a child without ascertaining the cause of his failures, and the fact that a child has a certificate of insusceptibility does not absolve its guardians from the duty of having the reality of the conditions tested from time to time."

Dr. Bory says[5] upon this point: "Of my own vaccinations, I may say that I have in my time performed over thirty-eight thousand primary operations with human or with calf lymph, and that it has only once fallen to my lot to fail twice at an attempt at vaccination. This subject was a ten-year-old child, in whom, as stated by its mother, vaccination had been attempted on previous occasions without result. My operation failed at the second attempt, and I did not get the opportunity to try a third time."

Dr. Thorne, chief medical officer of the Local Government Board, says[6]: "I would point out that the number of consecutive primary vaccinations by the board's own officers, without the occurrence of a single instance of so-called insusceptibility, now reaches 107,180."

The Technique of Vaccination.—Since vaccination with humanized lymph has been generally superseded by the use of vaccine from the calf it is unnecessary to present detailed instructions for collecting lymph from the arms of infants. Direct vaccination from arm to arm, with fresh fluid lymph, is superior to any other form of humanized vaccination, and should be performed when it is impracticable to obtain bovine virus.

Methods of Inserting Lymph.—The methods of insertion of either form of vaccine material are the same. The essential characteristics of a successful insertion are that the vaccine collected at the proper period of maturity should penetrate the superficial layer of the skin and be brought in contact with the rete Malpighii, or mucous layer. Bousquet states that smallpox was thus inoculated by Eastern nations in early periods.

The part usually selected for insertion is the outer part of the arm, at or near the lower insertion of the deltoid muscle, the left arm being usually preferred. Successful vaccinations may be made upon any part of the body. Among females it is quite a common practice to make insertions upon the thigh. In the case of young infants there are decided objections to this method.

Number of Insertions.—At least two insertions should be made in every case, and there can be no valid objection to a greater number. Heim recommends six, three on each arm; Bousquet, six; and Steinbrenner ten, five on each arm. Warlomont recommends six, three on each arm, and that they be arranged triangularly in boys, and in a horizontal line in girls, at the distance of a thumb's-breadth apart. He adds: "If one desires to please the mothers and spare subsequent reproaches, he will ask the mothers to point out where they wish the insertions to be made; the horizontal arrangement allows concealment by a short sleeve."

The Age for Primary Vaccination.—In all cases vaccination should be performed in early infancy, health permitting. Young unvaccinated children are the chief sufferers from smallpox. (Statistics relative to this point will be introduced later on.) There is great risk in delaying the operation, especially in the cities and large towns. Seaton advises that plump and healthy children living in large towns should be vaccinated when they are

a month or six weeks old; and in more delicate children the operation might be postponed until they are two or three months of age; but all whose health does not offer some positive contraindication should be vaccinated by the age of three months.

The writer has, under conditions of special exposure to smallpox, vaccinated several infants within the first forty-eight hours after their birth, with perfect success, and with typical vesicles resulting.

Health of the Individual to be Vaccinated.—It is not essential that the persons who are to be vaccinated should be in robust health. They should, however, be free from any acute disease, and also from any severe chronic disease which would be likely to interfere with the regular course of the vaccine vesicle. Many diseases do not interfere at all with the progress of vaccination.

In many countries, and also in some of the United States, vaccination is made a statutory prerequisite to school attendance, and the important question occasionally arises, "Shall exception be made in the case of scholars suffering from ill health?" From the standpoint of public hygiene, it must be urged that such scholars constitute a public danger, and a constant menace to the community, and it may also be added that a scholar whose health is not sufficiently good to permit of vaccination is not, as a general rule, in a condition of health to endure the routine of school attendance, and should remain out of school until recovery will permit of both school attendance and vaccination.

Methods of Insertion.—For precautions to be taken at the time of vaccination see No. 6 of the following instructions of the Local Government Board of England.

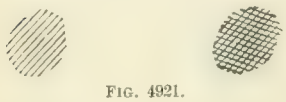

FIG. 4921.

1. One of the best methods, and also one most commonly employed, is the method of *scarification*. The arm of the person to be vaccinated should be grasped by one hand of the vaccinator, so as to put the skin upon the stretch. With a sharp lancet several fine parallel scratches, or incisions and cross incisions, should then be made upon the skin in the following manner (see Fig. 4921):

These incisions should be carried only to such a depth that the surface becomes slightly reddened by the appearance of blood. They may often be made upon sleeping children by means of a sharp lancet, without awakening them.

Several such scarifications should be made, never less than two, preferably of a smaller size than that which is shown in the cut, at a distance of about 1 in. (2–3 cm.) apart. Upon these should be applied the fresh lymph, rubbed lightly into the scarifications from the point of a lancet, and if preserved lymph is used, the contents of the tubes, points, or other appliances upon or in which it is stored should be transferred to the scarifications. If there is a free oozing of blood or serum, it is not necessary to moisten the dried lymph.

2. *Scraping.*—The outer skin may be scraped away with the edge of a sharp lancet over a surface 5–8 mm. in diameter, until a slight redness appears, but not sufficiently to induce a free oozing of blood. The lymph may be applied to this slightly reddened surface.

3. *By Puncture.*—By this method a sharp lancet is inserted obliquely to a depth of about one-eighth of an inch (2–3 mm.) or more. From two to five such punctures should be made at a distance of at least three-fourths of an inch apart. A common sharp-pointed lancet is best adapted to the purpose. The fresh lymph may be introduced into these punctures.

4. The method by puncture may be modified by making a considerable number of small punctures close together, or, in other words, a tattooing in several spots, the lymph being spread upon these spots.

The following are the revised instructions given by the Local Government Board of England to vaccinators under contract[7]:

1. Except so far as any immediate danger of smallpox may require, the public vaccinator must vaccinate only subjects who are in good health. As regards infants, he must ascertain that there is not any febrile state, nor any irritation of the bowels, nor any unhealthy state of the skin, especially no chafing or eczema behind the ears, or in the groin, or elsewhere in folds of skin. He must not, except of necessity, vaccinate in cases in which there has been recent exposure to the infection of measles, scarlatina, or diphtheria, nor in which erysipelas is prevailing about the place of residence.

2. A certificate of postponement must be given by the public vaccinator in the form prescribed by the Local Government Board or to the like effect: (*a*) If in his opinion the child is not in a fit and proper state to be vaccinated, or (*b*) if in his opinion the child cannot be safely vaccinated on account of the condition of the house in which it resides, or because there is or has been a recent prevalence of infectious disease in the district; and in any such case the public vaccinator is required forthwith to give notice of such certificate to the medical officer of health for the district in the proper form.

3. All public vaccinations are to be performed with glycerinated calf lymph or with such other lymph as may be issued by the Local Government Board. If the parent or other person having the custody of the child requires that it shall be vaccinated with lymph issued by the Local Government Board, the vaccination must be performed with such lymph.

4. The public vaccinator must keep such record of the lymph he uses for vaccinating as will enable him always to identify the origin of the lymph used in each operation. He must not employ lymph supplied by any person who does not keep an exact record of its source.

5. The public vaccinator must keep in good condition the lancets or other instruments which he uses for vaccinating, and he must not use them for any other purpose whatever. When he vaccinates he must cleanse and sterilize his instrument after one operation before proceeding to another, and must always, when vaccinating, have with him the means of doing this. When once he has unsealed a tube of lymph he must never attempt to keep any part of its contents for the purpose of vaccination on a future occasion. Under no circumstances should the mouth be applied directly to the tube in which the lymph is contained for the purpose of expelling the lymph. In the case of ordinary capillary tubes an artificial blower may properly be employed for this purpose.

6. Vaccination should at every stage be carried out with aseptic precautions. These should include: (1) The cleansing of the surface of the skin before vaccination; (2) the use of sterilized instruments; and (3) the protection of the vaccinated surface against extraneous infection both on the performance of the operation and on inspection of the results. Advice as to the precautions to be taken in this respect until the scabs have fallen and the arm has healed should always be given to the person having the custody of the child.

7. In all ordinary cases of primary vaccination the public vaccinator must aim at producing four separate good-sized vesicles, or groups of vesicles, not less than half an inch from one another. The total area of vesiculation resulting from the vaccination should not be less than half a square inch.

8. The public vaccinator must enter all cases in his register on the day when he vaccinates them, together with all particulars required in the register up to and including the column headed "Initials of the Person Performing the Vaccination." The results of the vaccination, which must be attested by the initials of the person who inspects the case, are to be entered upon the day of inspection. In cases of successful primary vaccination the public vaccinator must record the number of separate scarified areas, punctures, or groups of punctures made, and the number of separate normal vaccine vesicles or groups of vesicles which have been produced. In cases of revaccination, he must register as "successful" only those cases in which either vesicles, normal or

modified, or papules surrounded by areolæ have resulted. When any operation (whether vaccination or revaccination) has to be repeated owing to want of success in the first instance, it should be entered as a fresh case in the register.

Instruments Employed.—1. The common *lancet*, with a sharp point and edge, is undoubtedly the best instrument that has been devised for vaccination. It is simple, easily

FIG. 4922.—Vaccine Scarifier.

cleaned, easily sharpened, and may be used either for puncture or for scarification, the point being used for the former, and the edge for scarification.

2. *Needles.*—Steel needles or pins answer the same purpose, and may be easily cleansed either by heat or by disinfectants, or may be destroyed after each use.

3. Another instrument which proves quite efficient for scarification has the following shape. The only objection to this instrument is the greater difficulty in cleaning the spaces between the points (see Fig. 4922).

4. *Ivory Points.*—One of the advantages claimed for ivory or bone points is that they may serve two purposes: first, for the storage of lymph; and second for use in scarification, the edges near the point being sharpened or chamfered for the purpose (see Fig. 4923). They are poorly adapted for such use, it being impossible to give them a hard cutting edge as sharp as that of a lancet. In consequence of the porous quality of ivory and bone, and its consequent liability to retain pathogenic germs, an enterprising American firm has introduced a glass point with smooth surfaces, which may be used both for storage and for scarification.

FIG. 4923.—Ivory Point for Vaccine.

Various other instruments have been devised, many of them more or less complicated, and therefore not so well adapted for vaccination, in consequence of the greater difficulty in cleaning them, a point which deserves most careful attention in a matter of such great importance as that of vaccination.

Dr. Sagrandi, a surgeon of the Eleventh French Dragoons, has recently invented for use in vaccinating large numbers of people vaccinostyles or small metallic lances, one for each person vaccinated, which are sterilized by placing them to the number of fifty or more in racks in a small metallic cylinder, which is put into a larger cylinder containing a two-per-cent. solution of borate of soda, which is kept at the boiling point by a spirit lamp. This method has the advantage of rapidity and complete sterilization.

Dr. Burdon Sanderson employs a gauge for measuring vaccine vesicles (which is of the following shape), and estimates their protective value by the aggregate area of surface foveated in a characteristic manner. (Sixth Report of the Privy Council of England, p. 205.) (See Fig. 4924.)

Lymph which has been stored upon points for a month or more will often produce small vesicles, not more than 4–6 mm. ($\frac{1}{8}$–$\frac{3}{16}$ inch) in diameter, with very slight areola, but otherwise characteristic. The protective power of such a vaccination would presumably be but slight, and the vaccination should be repeated with fresh lymph.

Care of Instruments.—In consequence of the importance of this operation, it should invariably be performed with scrupulous regard to cleanliness. The instruments employed should be used for no other purpose, and if lancets are used, they should be cleaned with the greatest care after each use, and when several persons are to be vaccinated at once the instrument employed should be thoroughly sterilized after each operation. The use of a disinfecting solution for such purpose is desirable, such as a five-per-cent. solution of carbolic acid, or the flame of a spirit lamp.

Circumstances Calling for the Immediate Performance of Vaccination.—Under certain conditions it may be prudent to vaccinate at a very early age. When smallpox is prevalent in any locality, and especially when it exists in the same house where unvaccinated persons or such as have not been recently vaccinated are living, vaccination should be immediately performed. Repeatedly, for want of such precaution, have the lives of infants been sacrificed. The loss of a single day may sometimes prove to be the loss of a life.

Since the incubative period of vaccinia is shorter than that of smallpox by about three days, it is found that if vaccination is performed at any time within the first three days of exposure the vaccination will cause a certain degree of modification of the smallpox, and consequent protection. If it is postponed to a later day no protection is afforded. An illustration of the latter condition has come under the writer's observation. An unvaccinated child was exposed to smallpox on a certain day. Vaccination was delayed until ten days afterward. On the third day after the vaccination was performed, a well-marked eruption of smallpox appeared and the child died. Singularly enough the appearance of smallpox was attributed by some to the vaccine virus employed but two days previously.

The only safe rule under all such circumstances is to *vaccinate immediately.*

In all such cases it is of the utmost importance that accurate observations should be made and recorded as to the date of exposure, the date of vaccination, and also the date of the first symptoms of smallpox, should they occur.

Seaton also urges with propriety that the word "vaccinated" should not be used in certificates of death in which vaccination was merely attempted, but without any result. He also condemns in the strongest terms the practice of vaccinating after symptoms of smallpox have actually appeared in any given case presented for vaccination.

EXTENT TO WHICH VACCINATION IS NOW PRACTISED.—Jenner stated in 1801 that about six thousand persons had been inoculated with cowpox in England. In the previous year the practice of vaccination had been introduced into several other countries, and gradually won its way into public favor. At the present day a fair estimate of the annual number of vaccinations performed throughout the world (including revaccinations) may be stated to be at least thirty millions, which would amount to sixty per cent. of an estimated annual number of births of fifty millions. The ratio, however, has been constantly increasing, as the practice of vaccination has spread to countries where it had not been introduced.

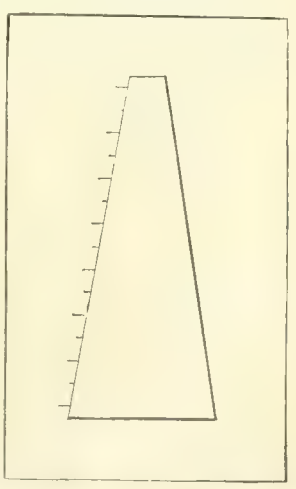

FIG. 4924.—Burdon Sanderson's Gauge for Measuring Vaccine Vesicles.

In the accompanying table the statistics of vaccination of several countries are presented, as compiled from such official sources as are accessible. It is to be regretted that the relative figures in the statistics of Scotland, England, Austria, and India have so little relation to each other. This fact is due to the lack of uniformity in the methods of reporting such statistics in different countries.

VACCINATION IN DIFFERENT COUNTRIES.

Years.	THE GERMAN EMPIRE.[1]	SCOTLAND.[2]		HOLLAND.[3]	DUTCH COLONIES.[3]	ENGLAND.[4]		JAPAN.[5]	AUSTRIA.[6]		BRITISH INDIA.[7]	
	Number of Vaccinations.	Successful Vaccinations.	Per cent. of births.	Vaccinations.	Vaccinations and revaccinations.	Successful vaccinations of children.	Per cent of children not accounted for.	Vaccinations.	Vaccinations.	Per cent. of living born.	Successful vaccinations.	Per 1,000 of the total population vaccinated.
1885	.....	.....	....	.....	1,407,927	757,714	5.8	4,325,437	678,677	77.3	4,703,214	
1886	.....	110,864	86.6	.....	1,307,239	754,059	6.4	5,842,447	691,460	80.3	4,950,893	
1887	.....	107,077	86.0	.....	1,378,470	733,980	7.1	3,066,491	694,357	79.3	5,202,595	
1888	2,487,484	106,734	86.6	.....	1,810,131	719,103	8.5	2,930,239	727,802	82.0	5,640,967	
1889	2,485,485	104,931	85.4	.....	1,297,703	707,161	9.9	1,970,292	703,897	79.1	5,709,462	25.7
1890	2,463,268	103,635	85.2	112,594	1,354,801	682,560	11.3	1,985,580	710,034	79.0	5,974,598	28.9
1891	2,462,603	107,482	85.3	118,209	1,424,923	693,117	13.4	2,224,791	768,621	88.4	5,882,683	26.8
1892	2,444,821	107,352	85.8	128,756	1,482,929	663,657	14.9	6,086,472	816,767	88.8	6,396,480	27.5
1893	2,433,779	108,117	85.0	123,870	1,903,001	661,513	16.1	7,994,702	751,780	83.8	6,716,134	28.9
1894	2,534,040	106,840	85.8	163,412	1,873,680	626,126	19.2	4,225,927	749,708	81.2	6,869,271	30.3
1895	2,513,900	108,035	85.7	109,194	1,536,571	624,690	20.5	2,848,646	734,069	81.4	7,223,591	32.0
1896	2,533,227	110,033	85.1	117,653	1,830,071	602,922	22.9	4,679,232	763,864	87.1	7,309,087	32.2
1897	2,630,176	108,378	84.0	119,830	1,736,041	578,639	22.7	15,701,684	742,200	78.2	7,144,474	31.5
1898	2,676,015	108,981	83.2	124,257	2,265,721	562,737	21.5	.....	734,989	77.8	6,860,915	30.2
1899	2,735,923	109,261	85.5	125,709	2,838,343	617,113	17.2	.....	.....	.....	7,437,916	32.9
1900	2,764,778	111,487	84.8	129,000	3,244,236	.....	....	.....	.....	.....	7,863,711	31.8

[1] Germany. "Die Ergebnisse des Impfgeschäfts im Deutschen Reiche," 1888–1900.
[2] Scotland. Reports of the Registrar-General of Scotland, 1886–1900.
[3] Holland. Reports of the Central Bureau of Statistics, 1900, p. 14.
[4] England. Reports of the Local Government Board, 1885–1900.
[5] Japan. Reports of the Central Sanitary Bureau, 1885–1897.
[6] Austria. "Oesterreichisches statist. Handbuch," 1885–1900. Also, "Statist. Sanitätswesen," Wien, 1901.
[7] British India. Reports upon the Sanitary Measures in India, 1885–1900.

The figures in the foregoing table are those of vaccinations performed by public officials only, and do not include many which are done by private practitioners. Such figures are obtainable only in countries where the value of such information is properly estimated. Unfortunately, in the United States, as a general rule careful records of vaccination are not kept, except in a few cities, and but little is known as to the number or the results of the vaccinations made in each year.

In every case the record should not be considered complete unless it contains at least the name and address of the person vaccinated, and the results of an inspection made within ten days afterward.

The blank form on the opposite page, simplified from those now used in England, gives the essential items necessary for a public record of vaccination.

In the following table are presented from official sources the numbers of vaccinations and revaccinations in several foreign cities mostly for the five years 1895–99.

VACCINATIONS IN LARGE CITIES, FIVE YEARS 1895–1899.

	Living births.	Primary vaccinations.	Re-vaccinations.	Total vaccinations.	Primary vaccinations. Per cent. of living births.
London[1] (1895–99)	668,012	400,502	.....	400,502	59.9
Paris[2] (1895–99)	293,375	178,419	256,849	435,268	60.8
Vienna[3] (1895–99)	125,500	110,689	30,837	141,526	88.2
Budapest[4] (1895–98)	88,319	92,970	42,011	134,981	105.3
Milan[5] (1898–99)	24,896	18,069	41,240	59,309	72.6

[1] Reports of Local Government Board, 1895–1900.
[2] Annuaire Statistique, Paris, 1895–99.
[3] Statistisches Jahrbuch.
[4] Statistisches Jahrbuch.
[5] Municipio di Milano. Dati Statistici, 1900.

The foregoing figures relate to official vaccinations performed and recorded by official vaccinators; except in Vienna, where vaccinations performed and reported by private physicians are also included.

After deducting those infants who died unvaccinated, there still remained in London and Paris a large unvaccinated infantile population.

In the figures for primary vaccinations in Budapest a considerable number of older persons appear to be included, so that the number of vaccinations exceeds that of living births.

The vaccinations in Paris are reported by the following authorities: By thirty-four hospitals and asylums, by bureaus of charity, by the Academy of Medicine, by the general sanitary inspection service, and by those having in charge infants supported at public cost.

Germany has at the present day the most thoroughly vaccinated population in the world, since the compulsory law of that country is the most efficiently enforced.

The following figures present the numbers of the vaccinated and revaccinated for the year 1900.[8]

Total number liable to vaccination	3,101,465
Total number liable to primary vaccination after excluding exempts	1,739,968
Total number liable to revaccination	1,281,039
Total	3,021,007
Total number vaccinated (primary)	1,518,510
Total number revaccinated	1,246,268
	2,764,778

Of these 99.94 per cent. were vaccinated with calf lymph and only 0.05 of one per cent. were vaccinated with humanized lymph. Glycerinated calf lymph was used in 1,485,522 of the primary vaccinations and also in 1,218,243 of the revaccinations. (For further figures see table at the top of this page.)

England.—In England in 1899 the statistics were as follows:

Number of births	929,189
Number successfully vaccinated	617,113
Reported as insusceptible	5,379
Had smallpox	4
Number in respect of whom certificates of conscientious objection have been received, under law of 1898	33,573
Died unvaccinated	113,516
Vaccinations postponed	16,605
Remaining	142,999

The percentage of children not accounted for, as compared with the births, was 17.2, that of 1898 having been 21.5.

Japan.—The following table presents the number of vaccinations in Japan in 1897 (the latest publication of the Central Sanitary Bureau).[9]

TOTAL VACCINATIONS IN JAPAN IN 1897.

	Successful.	Unsuccessful.
Primary	1,259,796	411,869
Revaccinations	4,458,265	9,571,754
Total	5,718,061	9,983,623

The success ratio of primary vaccinations was 75.3, that of revaccinations 31.8 per cent.

RECORD OF VACCINATION.

To be filled on the day of Vaccination.

RECORD OF VACCINATION.

To be filled on the day of Inspection.

1. Number.	2. Date of Vaccination.	3. Name of Vaccinated Person.	4. In case of Revaccination at ages over ten years, of persons previously successfully vaccinated, mark R.	5. Age. Yrs.	5. Age. Mos.	6. Residence. (Street and Number.)	7. Source of Lymph. Name of Producer.	8. Number of separate scarified areas or punctures made.	9. Initials of Vaccinator.	10. Date of Inspection.	11. Result. Successful, number of separate Vesicles produced.	11. Result. Unsuccessful.	12. Initials of Inspector.	13. Certificate of School Vaccination given. Yes.	13. Certificate of School Vaccination given. No.	14. Remarks.
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These forms may be conveniently made into books of 100 or 200 in each, sufficient for 1,000 or 2,000 vaccinations. If made up in this manner, the columns should be wider than those shown in the sample, and a blank space of two inches should be left between columns nine and ten for the convenience of folding and binding, the fold being made at that point.

The whole number of primary vaccinations in Japan in the ten years 1887–96 was 11,726,601, and the revaccinations in the same time were 16,709,064, making a total of 28,435,665. The total number vaccinated in 1897 (15,701,684) was more than half as many as the sum of the vaccinations of the preceding ten years. This enormous number is accounted for in the official report as follows:

"The furious rage of smallpox, and the cheapness of the price of vaccine lymph sold by the government institutes encouraged vaccination, and the number of vaccinated persons was very numerous compared with that of preceding years."

Italy.—The following figures presenting the number of vaccinations in Italy in the five years 1889–93 are given in "La Legislation et l'administration sanitaire en Italie, Rome, 1894."

NUMBER OF VACCINATIONS IN ITALY, 1889–93.

1889 ..	1,194,390	1892	1,997,114
1890 ..	1,618,880	1893	2,353,716
1891 ..	1,930,502		

In many of the United States, in consequence either of the entire absence of laws relative to vaccination or on account of the lax enforcement of such as exist, it is probable that the ratio of vaccinations to births is less than that of most of the countries of Europe, unless a few cities of the former may be excepted in which efficient boards of health have enforced annual vaccinations and revaccinations.

A general vaccination was made by the State Board of Health of Illinois in 1882, in which 233,340 vaccinations were performed in a population of over 3,000,000 people. Of these, 153,936 were primary vaccinations and 79,404 were revaccinations; the former being about double the annual number of births, the latter being estimated at 25 per 1,000 of the population.

A publication issued by the State Board of Health of Tennessee, April 1st, 1902, estimates the number of persons in that State who had been vaccinated in the previous three years as 753,617, or 41 per cent. of the total population. Of the white population 36 per cent. had been vaccinated, and of the colored population 50 per cent.

For the three years ended February 19th, 1902, there had also been in the same State 13,106 reported cases of smallpox, with a mortality of only 276 deaths, or 2 per cent.

The following statement occurs in the Report of the Surgeon-General of the United States Army for the year ended June 30th, 1899:

The population of Porto Rico is about 900,000. Smallpox was of frequent occurrence. It was decided to vaccinate all who had not recently had smallpox. This was carried out rapidly and efficiently; 786,290 persons were vaccinated.

By an order of January 27th, 1899, every resident "who has not had smallpox was ordered to be vaccinated, and hereafter all infants before reaching the age of six months."

The vaccine lymph was produced from heifers reared upon the island, and the cost of the work was $28,536.17.

THE PROTECTIVE POWER OF VACCINATION. In order to consider this phase of the question intelligently, and to determine satisfactorily the protective value of vaccination and of revaccination against smallpox, it will be necessary to consider the subject: *first*, by a comparison of the period before, with the period following, the introduction of vaccination; *second* (since it may with reason be urged that epidemics of several infectious diseases have become less severe within a century or more), a comparison of different populations living under similar conditions, except that of vaccination; and *third*, a consideration of the effect of vaccination upon the age-distribution of smallpox.

1. *The Period Before and the Period After the Introduction of Vaccination.*—It will be necessary in this connec-

tion to review the history of smallpox, for a century or more, in different countries.

"At the present day," says Simon, "the very success of vaccination may have blinded people to its importance. It is very easy to be bold against an absent danger, to despise the antidote while one has no painful experience of the bane."

Smallpox is fatal to a large proportion of those whom it attacks; it is eminently infectious from person to person; it seizes, with very few exceptions, upon all unvaccinated persons who for the first time come within its range.

Although smallpox has been described with accuracy by early writers, notably by the Arabian physician Rhazes, its history previous to the eighteenth century must be regarded as in a great measure defective, in consequence of being confounded with measles and with other diseases.

It is known that not a decade passed in the seventeenth and eighteenth centuries without the occurrence of devastating epidemics of smallpox in Europe. In England from seven to nine per cent. of all deaths were attributable to smallpox. In London it averaged from four to eight per cent. of the total deaths. Capt. John Graunt, in his observations on the Bills of Mortality of London (published in 1665), gives the number of deaths from smallpox for twenty years (1629 to 1636, 1647 to 1658), as 10,576, out of a total mortality of 229,250. It was also the seventh in the order of destructiveness upon the population, consumption being first.

In Berlin, from 1783 to 1797, one-twelfth of all deaths, according to Casper, were from smallpox. M. de la Condamine estimates that one-tenth of all deaths in France, amounting to 30,000 annually, were from smallpox. Three and a half millions perished from it in Mexico in the sixeenth century. In 1734 nearly two-thirds of the population of Greenland were swept away by it. In Iceland 18,000, out of a population of 50,000, died of smallpox. Catlin, in his "Letters and Notes on the Manners and Customs of the North American Indians," says: "I would venture the assertion, from books that I have read and from other evidence, that of the numerous tribes that have already disappeared, and of those that have been traded with, quite to the Rocky Mountains, each one has had this exotic disease in their turn, and in a few months have lost one-half or more of their numbers."

Wernher says, in his recent work, "Zur Impffrage": "Before the introduction of vaccination smallpox had become a permanent disease which never entirely ceased in one year, and every three or five years became a great epidemic.

"In non-epidemic years one-tenth of all mortality was from variola, in epidemic years one-half. Very few men escaped smallpox till old age; almost every one sickened at least once in his life of this horrible, murderous disease.

"Countless mortals who escaped death were maimed by loss of sight. Of new-born children, one-third died of smallpox before their first year; one-half before their fifth year of life. There was no family which had not heavy losses to deplore. In the country the mortality was greater than it was in the city.

"Physicians and Government possessed no means against this abominable evil. Isolation was impracticable from the general, widespread nature of the disease. Men accepted the pest as an unavoidable fate.

"The loss which Europe suffered from this one disease amounted to many millions. It was a principal factor which deterred or kept the population from progress; and to lead us back to these conditions are the efforts of many ignorant mortals directed."

Comparing the present conditions with those just stated the author goes on to say:

"We now find no child mortality from smallpox among vaccinated children.

"Also, among adults, whenever vaccination and revaccination are maintained, mortality from smallpox is at an end."

The following familiar table is herewith quoted from the "Report of the Epidemiological Society of London," and contains very conclusive evidence of the decline of smallpox in different countries after the introduction of vaccination. Two series of facts are presented. (1) The number of persons per million of the population who died of smallpox annually *before* the introduction of vaccination; and (2) the number per million who died annually of the same disease after its introduction. The periods are not in all cases the same, but the statistics are those which it was possible to collect for the periods named.

Period relative to which data are given.	Country or city.	Approximate Average Annual Death Rate by Smallpox per Million Inhabitants.	
		Before introduction of vaccination.	After introduction of vaccination.
1777 1806 and 1807 1850.	Lower Austria	2,484	340
1777-1806 and 1807 1850.	Upper Austria, and Salzburg	1,421	501
1777-1806 and 1807-1850.	Styria	1,052	446
1777-1806 and 1807-1850.	Illyria	518	244
1777-1806 and 1838-1850.	Triest	14,046	182
1777-1803 and 1807-1850.	Tyrol and Voralberg	911	179
1777-1806 and 1807 1850.	Bohemia	2,174	215
1777-1806 and 1807-1850.	Moravia	5,402	255
1777 1806 and 1807-1850.	Silesia (Austrian) ..	5,812	198
1777-1806 and 1807-1850.	Galicia	1,194	676
1787 1806 and 1807 1850.	Bukowina	3,527	516
1776-1780 and 1810-1850.	Prussia (Eastern) ..	3,321	56
1780 and 1810-1850.	Prussia (Western) .	2,272	356
1780 and 1816-1850.	Posen	1,911	743
1776-1780 and 1810-1850.	Brandenburg	2,181	181
1776-1780 and 1816-1850.	Westphalia	2,643	114
1776-1780 and 1816-1850.	Rhenish Provinces.	908	90
1781-1805 and 1810-1850.	Berlin	3,422	176
1776-1780 and 1816-1850.	Saxony (Prussian) .	719	170
1780 and 1810 1850.	Pomerania	1,774	130
1774-1801 and 1810-1850.	Sweden	2,050	158
1751-1800 and 1801-1850.	Copenhagen	3,128	286

In the accompanying chart (Fig. 4925) are also presented the data relative to the mortality from smallpox in Sweden before and after the introduction of vaccination, by which it appears that in the twenty-four years before the introduction of vaccination in 1801 the mortality from smallpox counted 2,050 victims annually out of each million of the population, and after the introduction of vaccination this mortality was reduced to 158 per million annually. The period anterior to 1773, included in the original, has been omitted, since the deaths from smallpox previous to that year were not separated from those from measles.

No complete statistics of American cities for the period before the introduction of vaccination can be obtained. The data contained in the accompanying table are compiled from the most reliable historical sources, with reference to the prevalence of smallpox in Boston.

After the settlement of the colony at Plymouth, in 1620, smallpox appeared frequently in Massachusetts, among both the Indian tribes and the English settlers. Such epidemics occurred in 1631, 1633, 1639, 1677, 1678 (from 700 to 800 died in this year), 1702 (213 died, which was about 4.4 per cent. of the population). In 1721, with a population of 11,000, there were in Boston 5,989 cases of smallpox, more than half the population taking the disease, of which number 850 died. In the words of the historian: "The disease ran riot over the town, feasting on all who were susceptible to its poison" (Dr. Toner, in publications of Mass. Med. Soc., 1866, vol. ii.).

In 1730, with a population of 15,000 people, 4,000 were sick, and about 500 died. A vessel from London, with smallpox on board, was wrecked in 1751 near Nahant, and spread the disease again, and there were 7,653 cases, and 545 deaths. It broke out in the American army at

Cambridge in 1776, and Dr. Waterhouse wrote "There were scarcely enough men free from it, or not liable to take it, to keep guard at the different hospitals."

In 1792, 8,346 had smallpox. In this epidemic it is stated that, out of a population of 19,484, 10,655 had already had smallpox, and that only 221 persons escaped having it, the remainder having moved out of town.

So virulent did it at times become as to compel the legislature to hold its sessions in some other town (Report of State Sanitary Commission of 1850, pp. 64–70).

After the introduction of vaccination the mortality from smallpox in Boston was as follows, so far as the records can be obtained:

	Deaths.		Deaths.
From 1811 to 1820	6	From 1861 to 1870	500
From 1821 to 1830	8	From 1871 to 1880.....	1,094
From 1831 to 1840	214	From 1881 to 1890....	24
From 1841 to 1850	534	From 1891 to 1900.. .	32
From 1851 to 1860	732	For 1901 and 1902. ..	267

By reference to the tables relative to the prevalence of smallpox, which for the eighteenth century present only the date of epidemic years, since other data are not to be had, it will be seen that the highest ratio of deaths from smallpox, in any epidemic year since the introduction of vaccination (2.95 per 1,000 of the living population), was much less than that of the lowest epidemic year before its introduction.

Among the few records as to the prevalence of smallpox before the general introduction of vaccination, one of the best is found in a recent paper by Dr. John C. McVail, of Kilmarnock, Scotland, published in 1882 (Fourteenth Report of Medical Officer of the Local Government Board of England, p. 39). It presents a most graphic picture of the prevalence of smallpox at that time. It appears that a schoolmaster of Kilmarnock,

SMALLPOX IN BOSTON BEFORE THE INTRODUCTION OF VACCINATION. EPIDEMIC YEARS ONLY.

Year.	Population.	Cases of smallpox.	Deaths from smallpox.	Death rate from smallpox per 1,000 inhabitants.	Remarks.
1631 [1]	.....	....	Very many.		
1633 [2]	.....	....	Very many.		
1639 [3]	150	....	Very many.		
1677 [4]	4,000	....	Very many.		
1678 [5]	4,000	....	Very many.	....	700-800 died in Massachusetts, exclusive of blacks.
1702 [6]	6,750	....	213	31.5	
1721..	11,000	6,006	850	77.3	Inoculation introduced.
1730..	15,000	4,000	500	33.3	
1752..	15,731	7,669	569	36.2	
1764..	15,520	5,646	170	10.9	
1776 [6]	5,750	5,292	57	10.0	
1778 [6]	10,000	2,243	61	6.1	
1792..	20,000	8,346	198	9.9	

[1] Increase Mather. [2] Report of Sanitary Commission, 1850.
[3] Webster's History of Pestilence. [4] Charlestown Records.
[5] Felt: Annals of Salem. [6] Population changeable; years of war.

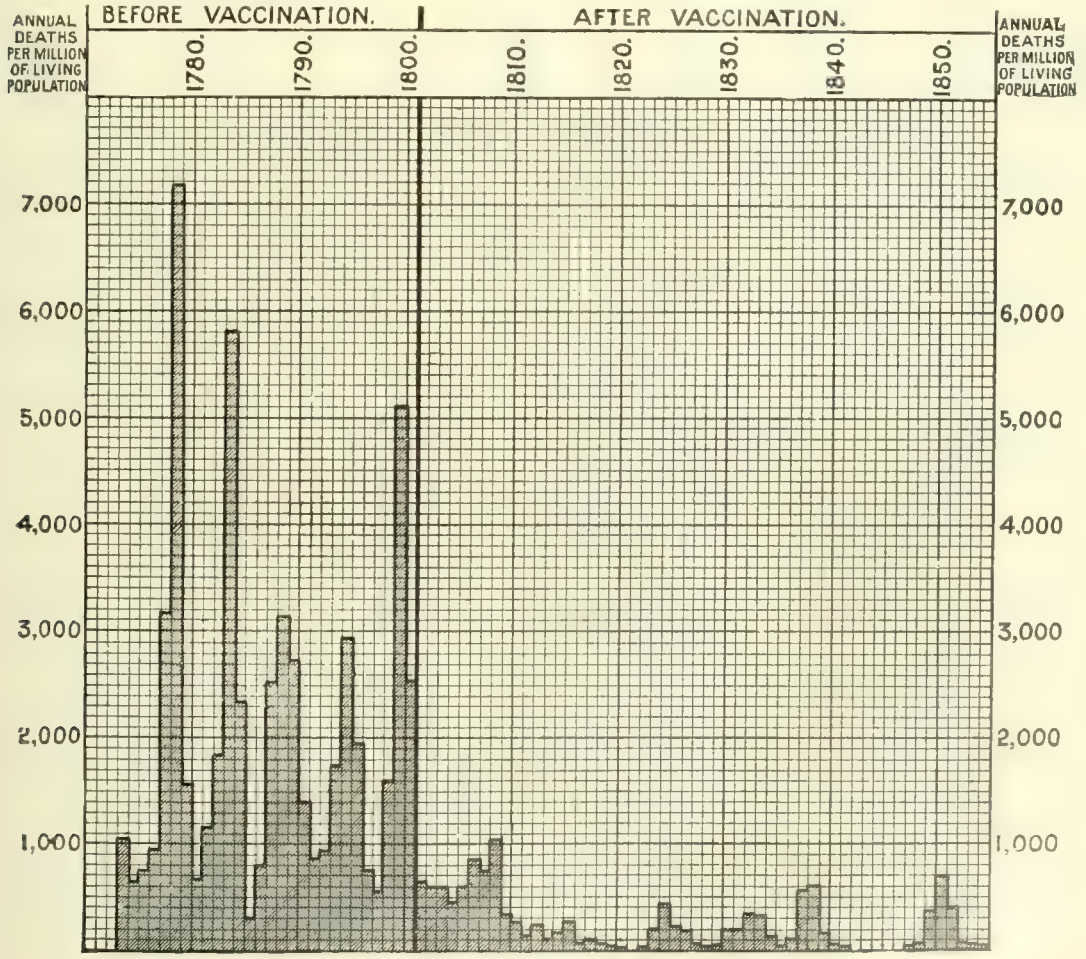

FIG. 4925.—Death Rates from Smallpox in Sweden, 1773-1855.

SMALLPOX IN BOSTON AFTER INTRODUCTION OF VACCINATION.

Year.	Population	Cases of Smallpox.	Deaths from Smallpox.	Death rate per 1,000 inhabitants.	Year.	Population.	Cases of Smallpox.	Death from Smallpox.	Death rate per 1,000 inhabitants.
1811.	33,000		2	0.05	1857	.....	....	2	0.01
1812.	.....		....	....	1858	.....	....	3	.02
1813.	.....		...	....	1859	.....	....	156	.97
1814.	.....		....	....	1860	177,840	....	162	.92
1815.	.....		4	.12	1861	.....	....	7	.04
1816.	.....		....	....	1862	.....	....	13	.07
1817.	.....		....	....	1863	.....	....	11	.06
1818.	.....		....	....	1864	.....	....	113	.63
1819.	.....		....	....	1865	192,318	....	115	.60
1820.	43,298		....	....	1866	.....	....	51	.26
1821.	.....		....	....	1867	.....	....	144	.75
1822.	.....		....	....	1868	.....	....	8	.04
1823.	.....		....	....	1869	.....	....	6	.03
1824.	.....		1	.02	1870	250,526	....	32	.13
1825.	58,277		1	.017	1871	.....	....	28	.11
1826.	.....		....	....	1872	.....	2,592	738	2.95
1827.	.....		3	.05	1873	.....	1,103	302	1.21
1828.	.....		2	.03	1874	.....	3	2	.008
1829.	.....		....	....	1875	341,919	7	1	.003
1830.	61,392		....	....	1876	.....	1	2	.006
1831.	.....		4	.06	1877	.....	...	4	.012
1832.	.....		2	.03	1878	...	....	....	...
1833.	.....	No record.	....	....	1879	.....	....	....	....
1834.	.....		4	.05	1880	362,839	7	1	.003
1835.	78,653		7	.10	1881	.....	44	6	.017
1836.	.....		6	.09	1882	.....	24	8	.022
1837.	.....		13	.16	1883	.....	8	1	.003
1838.	.....		3	.04	1884	.....	1	1	.003
1839.	.....		60	.09	1885	390,393	11	2	.005
1840.	93,383		115	1.23	1886	.....	1	....	....
1841.	.....		57	.61	1887	.....	4		....
1842.	.....		42	.45	1888	.....	8	1	.002
1843.	.....		55	.06	1889	.....	10	2	.005
1844.	.....		....	....	1890	448,477	1	....	....
1845.	114,366		31	.27	1891	.....	....	....	....
1846.	.....		92	.81	1892		....	....	....
1847.	.....		23	.20	1893	.....	26	4	.008
1848.	.....		21	.19	1894	.....	77	22	.045
1849.	.....		21	.19	1895	496,920	....	....	....
1850.	136,881		192	1.40	1896	.....	...	....	...
1851.	.....		63	.46	1897	.....	10	....	....
1852.	.....		12	.09	1898		....	...	....
1853.	.....		6	.04	1899	.....	29	5	.010
1854.	.....		118	.86	1900	560,892	7	....	....
1855.	160,490		132	.80	1901	.....	504	79	.14
1856.	.....		78	.49	1902	.....	1,024	188	.32

who was considerably in advance of his times, kept a record of the mortality of his parish in a beautifully written volume. This schoolmaster, Robert Montgomerie, was also the session clerk. The record contains a statement of the name, date, age, and cause of death of all who died in the parish of Kilmarnock for the thirty-six years from March 1st, 1728, to March 1st, 1764.

The population of the town in question is estimated to have averaged 4,200 for the period under consideration. The total deaths for the thirty-six years were 3,860, which would indicate a death rate of 24.36 per 1,000 per annum. In the careful record of the schoolmaster, which is divided into groups of six years each, four causes are credited with fully two-thirds of the total deaths. These were decay, age, smallpox, and fevers. What is meant by decay it is not easy to state; that old age is not a necessary element is evident from the fact that deaths at the ages of one and two years are attributed to it. The term embraces nearly all chronic diseases causing emaciation and debility, among which, of course, consumption is chief. From such cause or causes there were 915 deaths. The second disease was age, with 625 deaths, which appears to have formed a convenient class for all persons who lived beyond seventy years, and for many between sixty and seventy years. Omitting smallpox, fevers were credited with 545 deaths. This term probably included scarlet fever, which is not mentioned elsewhere, and also, perhaps, pneumonia and other acute febrile diseases.

There can be no doubt, says Dr. McVail, that smallpox caused more deaths, by a long way, than any other disease in old Kilmarnock. The entire number of deaths from smallpox in this little parish for the thirty-six years was 622. There were in all nine epidemics in the thirty-six years, the average time between the epidemics being four years. They came with terrible regularity.

The following table presents the data of these epidemics of smallpox by years and by ages:

Year.	Total deaths.	Age in Years at Death.							Age not stated.
		Under 1.	1.	2.	3.	4.	5.	6 and over.	
1728	66	7	14	12	14	9	5	4	..
1729									
1730	..	..	..	..	..	..	..	.	1
1731	..	..	..	..	..	..	..	..	..
1732	..	..	..	..	..	..	..	..	..
1733	45	12	9	13	6	4	..	1	..
1734	..	..	..	..	..	..	..	..	..
1735	..	..	..	..	..	..	..	..	..
1736	66	12	20	20	8	1	1	4	..
1737	..	..	..	..	..	..	..	..	..
1738	..	..	..	..	..	..	..	..	..
1739	..	..	..	..	..	..	..	..	..
1740	66	15	21	9	14	2	2	2	1
1741	..	..	..	..	..	..	..	..	..
1742	..	..	..	..	..	..	..	..	..
1743	..	..	..	..	..	..	..	..	..
1744	74	15	13	19	11	10	2	3	1
1745									
1746	8	3	2	1	1	..	..	1	..
1747	..	..	..	..	..	..	..	..	..
1748	2	.	..	1	1	..	..	..	..
1749	84	12	17	22	15	12	..	5	1
1750									
1751	1	..	..	..	1	..	..	..	..
1752	..	..	..	..	..	..	..	..	..
1753	1	1	..	..	..	..	..	..	..
1754	95	23	25	15	15	10	5	2	..
1755	..	..	..	..	..	..	..	..	..
1756	..	..	..	..	..	..	..	..	..
1757	46	11	11	13	6	4	1	..	2
1758									
1759	..	..	..	..	..	..	..	..	
1760	..	..	..	..	..	..	..	..	..
1761	..	..	..	..	..	..	..	..	..
1762	66	7	7	10	9	10	8	4	3
1763	2	..	..	1	..	..	..	1	..
Totals	622	118	139	136	101	62	24	27	9

In seven of these nine epidemics the death rate for the year was higher than the birth rate, in one year to the extent of seventy-two per cent. The statistics of these years are summed up in the following table:

EPIDEMIC YEARS IN WHICH THE TOTAL DEATHS EXCEEDED THE TOTAL BIRTHS.

Year.	Births.	Deaths from all causes.	Deaths from smallpox.	Excess of deaths over births.
1728-29	111	162	66	51
1736-37	135	147	66	12
1740-41	95	164	65	69
1749-50	134	149	79	15
1754-55	146	203	95	57
1757-58	125	132	37	7
1762-63	132	173	66	41
Total	878	1,130	474	252

It will prove instructive to compare the greatest epidemic of modern times, in the same town, with the greatest to be found in the old records. In the year 1874 there were 141 deaths from smallpox in Kilmarnock, which then had 24,000 inhabitants, or at the rate of 5.8 per 1,000 living. The old epidemic was, therefore, four times as severe as the modern one, and it should be remembered that while the former epidemic had only a period of four and a half years in which to collect its victims, no serious epidemic had occurred for more than thirty years previous to 1874. One can hardly conceive what would be said at the present day about an ordinary annual death rate as great as that of what we have learned to look upon as a terrible epidemic, and yet an annual epidemic equal to that of 1872–73 would do little more than represent the conditions which prevailed in the eighteenth

century. Similar statistics for other English towns confirm these statements of Dr. McVail.

2. *Comparison of the Vaccinated with the Unvaccinated in Like Periods of Time.*—If, now, it shall be urged, as it is occasionally, with some degree of reason, that certain malignant diseases have almost disappeared, at least from among civilized nations, and that the disappearance, or comparative rarity, of smallpox is not a necessary consequence of vaccination, let us then examine the condition of the vaccinated, as compared with that of the unvaccinated, with reference to their immunity from smallpox, while living in a similar environment and at the same period of time.

Wherever extensive parallel observations are made upon large populations of the vaccinated and of the unvaccinated, as exposed to epidemics of smallpox, the protective power of vaccination is especially manifest.

In the accompanying table are given the statistics of different populations in which observations are made upon the comparative immunity from smallpox of the vaccinated and the unvaccinated. It will be noticed that in the majority of the instances noted, the mortality among the vaccinated was but one-fifth or one-sixth of that of the unvaccinated, and that the highest mortality among the vaccinated was less than the lowest among the unvaccinated.

Places and dates of observation.	Total number of cases observed.	Death Rate per 100 Cases	
		Among the unvaccinated.	Among the vaccinated
France,[1] 1816-41	16,397	16.1	1.0
Canton Vaud,[2] 1825-29	5,848	24.0	2.2
Verona,[3] 1828-30	969	46.6	5.6
Milan,[4] 1830-51	10,240	38.5	7.6
Breslau,[2] 1831-34	220	53.8	2.1
Württemberg,[5] 1831½-35½	1,442	27.3	7.1
Carniola,[6] 1834-35	442	16.2	4.4
Vienna Hospital,[2] 1834	360	51.2	12.5
Carinthia,[6] 1834-35	1,626	14.5	.5
Adriatic,[2] 1835	1,002	15.2	12.8
Lower Austria,[2] 1835	2,287	25.8	1.5
Bohemia,[7] 1835-55	15,640	29.8	5.2
Galicia,[2] 1836	1,059	23.5	5.1
Dalmatia,[2] 1836	725	19.6	8.2
London smallpox hospital,[7] 1836-56	9,000	35.0	7.0
Vienna Hospital,[7] 1837-56	6,213	30.0	5.0
Kiel,[7] 1852-53	218	32.0	6.0
Malta,[8]	7,570	21.1	4.2
Epidemiological Society Returns [8]	4,624	23.0	2.9
Illinois [9]	1,931	48.6	6.1
Leicester,[10] 1892-93	347	12.3	.8
Sheffield,[11] 1887-88	6,088[12]	32.6	4.9

[1] Wunderlich's Handbook, iv., 201.
[2] Steinbrenner.
[3] Rigoni-Stern: Die Vaccination und ihre neuesten Gegner, 1854.
[4] Canstatt's Jahresbericht, 1852.
[5] Heim.
[6] Med. Jahrb. d. Oesterr. Staates, 1838.
[7] Report of Coll. of Surgeons, and Statement of Professor Hebra.
[8] Seaton.
[9] Fifth Report of State Board of Health, 1882.
[10] Report on Epidemic of Smallpox, Leicester, 1893.
[11] Dr. Barry's Report, 1889.
[12] The deaths of the unvaccinated children under five years of age were 46.7 per cent. of those attacked, while those of the vaccinated children were only one per cent.

One of the most valuable reports of modern times, bearing upon the subject of the value of vaccination, is the report of Dr. F. Barry, upon the epidemic of smallpox in Sheffield, in 1887–88. Dr. Barry, an inspector of the Local Government Board of England, was instructed to inquire into every influence which could possibly bear upon the epidemic of smallpox at Sheffield. After making a most thorough and searching investigation, as his report shows, no influence could be discovered beyond the single dominating one of vaccination.

Dr. Buchanan's introductory to this report sums up the results as follows:

	Per 1,000 of each class stated.			
	Attack rate.		Death rate.	
	Vaccinated.	Unvaccinated.	Vaccinated.	Unvaccinated.
Up to ten years	5.0	101	0.09	44
Living in invaded houses	78.0	869	1.0	381
Over ten years	19.0	94	1.0	51
Living in invaded houses	281.0	686	14.0	371
All ages	15.5	97	1	48
Living in invaded houses	230.0	750	11.0	372

In the foregoing table the figures represent the rates per thousand of the child population under ten years, of persons over ten years of age and of persons of all ages; first, as applying to the population of the borough generally, and secondly, as applying to the enumerated population of the invaded houses. In a brief summary Dr. Buchanan further says, "the vaccinated children had, as compared with the unvaccinated in the same town, a twentyfold immunity from attack by smallpox, and had a four hundred and eightyfold security against death by smallpox; that in the invaded houses the vaccinated children had, as compared with the unvaccinated, an elevenfold immunity from attack by smallpox, and a three hundred and eighty-onefold security against death by smallpox, and that as regards all ages the vaccinated among the population generally had, as compared with the unvaccinated, a sixfold immunity against attack, and a sixty-fourfold security against death."

The following table presents the deaths and death rates from smallpox in those countries from which reports could be obtained. It shows, in general, in the lower table of relative figures the lower death rates from smallpox in well- or comparatively well-vaccinated countries. The figures for several years are not accessible in the reports of Japan, Italy, Hungary, and Spain. (See p. 126.)

Evidence was presented, for example, before the British Commission that there was but little opposition to vaccination in Scotland and Ireland as compared with that which existed in England. The result is apparent in the table.

Surgeon-General Sir William Moore testifies that the large yearly ratio of vaccination in India has had a very marked effect in the reduction of smallpox in that country.[37]

He also states his experience in India before vaccination had been generally introduced. He says he marched during an epidemic of smallpox a distance of one thousand miles, surrounded by smallpox. "Those suffering from the disease in a minor degree were in the streets, generally children, occupied in their accustomed play; or if too ill, lying neglected on the ground; and these represented a portion of the whole suffering from smallpox, the remainder, unable to leave their dwellings, awaiting death in their houses. Any one cognizant of the after-effects of smallpox will at once understand the amount of suffering which must occur among those recovering from the immediate disease. The consequent effects on the eyes, the ears, the skin, the limbs, the joints, and the general constitution, at least equal in gravity the direct consequences of the disease. Roughly speaking, from calculations based on observing the people passing through the streets of certain cities, ten per cent. had lost the sight of one or both eyes, and an equal number had permanent injury of some organ or member; and of these affections the great majority could be traced to smallpox. From special inquiry I found nearly eighty per cent. of the population were more or less marked with smallpox."

According to the *British Medical Journal* there were in the last epidemic of smallpox in Guatemala twenty-five thousand deaths from the disease. In that country there are no vaccination laws. Its population is about one-half as large as that of New England, in which there have not been so many smallpox deaths in the last sev-

enty-five years combined. The *Journal* characterizes Guatemala as an "antivaccination paradise" (*British Medical Journal*, 2, 1891, p. 1135).

At the Tenth International Medical Congress in Berlin, in 1890, Dr. Victor Desguin, of Antwerp, said that the medical inspection of schools in that city had been organized in a very complete manner since 1882, at which time revaccination was ordered for all school children who were twelve years old. It is performed with lymph, under every possible condition of security. It is furnished by the Central Vaccinal Institute of Belgium, and before delivery of the lymph an autopsy is made upon the animal from which it has been taken, to determine its condition of health, none being issued if the animal is found to be diseased. So that there is no danger of communicating either syphilis or tuberculosis.

DEATHS FROM SMALLPOX IN DIFFERENT COUNTRIES. ABSOLUTE AND RELATIVE FIGURES.

Absolute Figures.

Years.	Group I.								Group II.						
	German Empire.	Scotland.	Ireland.	Sweden.	Switzerland.	Holland.	Dutch Colonies.	England.	Italy.	Japan.	Belgium.	Austria.	British India.	Hungary.	Spain.
1880	....	10	389	175	173	79	...	648	....	8,210	4,135	14,232	69,849	13,386	12,165
1881	....	19	72	299	167	75	....	3,098	....	12,995	2,721	18,019	71,647	12,467	10,548
1882	....	3	129	159	22	153	....	1,317	....	41,849	1,570	21,154	85,148	12,160	19,933
1883	....	11	16	125	24	673	....	957	....	12,189	1,796	13,310	232,436	6,789	16,903
1884	....	14	1	58	64	62	....	2,234	....	.410	1,355	11,521	333,382	3,992	10,648
1885	....	39	4	4	426	31	....	2,827	....	3,329	1,636	13,212	80,785	4,746	
1886	197	24	2	2	182	72	....	275	....	18,676	1,213	8,794	51,112	11,290	
1887	168	8	14	5	14	18	....	506	16,249	9,967	610	9,591	65,757	15,740	
1888	112	3	3	9	17	1	....	1,026	18,110	853	865	14,138	93,568		
1889	200	8	0	2	3	10	....	23	13,416	328	1,212	12,358	125,453	....	8,472
1890	58	0	0	2	32	1	....	16	7,017	25	636	5,935	116,321	....	6,183
1891	49	0	7	2	26	10	....	49	2,910	721	1,300	6,838	93,745	....	9,081
1892	108	11	0	4	35	49	....	431	1,453	8,409	2,528	6,087	92,680	3,426	6,854
1893	157	68	1	25	15	190	363	1,457	2,638	11,852	2,103	5,821	63,178	1,224	5,194
1894	88	129	72	21	51	625	422	820	2,606	3,342	537	2,512	41,609		
1895	27	47	146	0	1	79	231	223	2,998	268	298	1,164	43,328		
1896	10	2	4	2	8	34	337	541	2,033	3,388	130	897	132,784		
1897	5	10	3	1	1	1	588	25	1,003	12,276	140	1,450	160,059		
1898	15	2	0	1	2	7	673	253	420	....	158	2,521	55,798		
1899	28	1	1	1	....	0	2,012	174	214	....	257	1,899	48,598		

DEATH RATES FROM SMALLPOX PER MILLION INHABITANTS.

Relative or Significant Figures.

Years.	Group I.								Group II.						
	German Empire.	Scotland.	Ireland.	Sweden.	Switzerland.	Holland.	Dutch Colonies.	England.	Italy.	Japan.	Belgium.	Austria.	British India.	Hungary.	Spain.
1880	...	2.8	75.0	38.0	61.0	19.0	....	25.0	....	322	749	647	356	853	724
1881	....	5.1	14.0	65.0	59.0	18.0	....	119.0	....	351	487	819	362	789	624
1882	....	.8	2.5	34.6	8.0	37.0	....	50.0	....	1,122	277	962	430	765	1,172
1883	....	3.0	3.2	27.2	9.0	160.0	....	36.0	....	327	314	605	1,174	424	988
1884	....	3.7	.2	12.6	22.0	15.0	....	83.0	....	11	234	523	1,650	245	619
1885	....	10.0	.8	.9	149.0	7.0	....	104.0	....	88	280	575	450	287	
1886	4.2	6.2	.4	.4	63.0	17.0	....	10.0	....	485	205	382	249	676	
1887	3.5	2.1	2.8	1.1	5.0	4.0	...	18.0	550	256	102	417	313	932	
1888	2.3	.8	.6	2.0	6.0	.2	....	36.0	610	22	144	615	445		
1889	4.1	2.0	....	.4	1.0	2.0	....	.8	449	8	199	515	570	....	481
1890	1.2	....	....	.4	11.0	.2	....	.6	233	6	105	247	529	....	350
1891	1.0	....	1.5	.4	9.0	2.0	....	1.7	96	18	212	285	426	....	508
1892	2.2	2.1	...	.9	12.0	11.0	....	15.0	48	205	408	253	403	193	381
1893	3.1	16.5	2.0	5.2	5.0	40.0	14.0	49.0	86	289	334	243	274	69	285
1894	1.7	31.5	15.7	4.4	16.0	131.0	16.0	27.0	85	80	85	102	181		
1895	.5	11.5	31.8	....	.3	16.0	9.0	7.0	97	6	47	47	188		
1896	.2	.5	.9	.4	2.5	7.0	13.0	18.0	65	81	20	36	577		
1897	.1	2.4	.6	.2	.3	.2	22.0	.8	32	284	21	57	696		
1898	.3	.5	....	.2	.6	1.4	24.0	8.0	13	....	24	98	243		
1899	.5	.2	.2	.2	....	....	72.0	5.0	7	....	38	73	211		
Mean of 20-year period	1.8	5.3	9.0	9.3	22.6	24.2	26.0	33.8	179	202	206	358	475	516	605

Sources of Information for the Foregoing Tables.

1. Germany. "Ergebnisse der amtlichen Pockentodesfallsstatistik im Deutschen Reiche," 1886–1899.
2. Scotland. Reports of the Registrar-General.
3. Ireland. Reports of the Registrar-General.
4. Sweden. "Bidrag till Sveriges Officiala Statistik," 1899.
5. Switzerland. "Statistisches Jahrbuch der Schweiz," 1900.
6. Holland. Annuaire statistique pour le Royaume des Pays-bas," 1899.
7. Dutch Colonies. "Annuaire statistique des Pays-Bas (Colonies)," 1899.
8. England. Reports of the Registrar-General, 1880–1899.
9. Italy. "Statistica delle cause de Morte," Rome, 1901, p. 12.
10. Japan. Reports of the Central Sanitary Bureau, Tokio, 1900.
11. Belgium. "Annuaire statistique de Belgique," 1901.
12. Austria. "Oesterreichisches statist. Handbuch," Wien, 1900.
13. British India. Annual Reports in the Sanitary Measures in India, 1880–1899.
14. Hungary. Bulletin de l'Institut International de Statistique, Rome, vol. x.
15. Spain. Bulletin de l'Institut International de Statistique, Rome, vol. x.

In nine years 15,259 children were vaccinated, of which 8,033, or 52 per cent., were successful. He says this ratio of success in revaccination is probably due to the fact that a considerable number of children enter the schools with false certificates of vaccination, either on account of inefficient performance or by reason of its omission.

Revaccination was not followed in any case by unusual results, beyond what could easily be controlled, the school registers giving the particulars as to absence in all cases.

Moreover, he says that revaccination was never followed by the development of scrofulous symptoms; a fact which he attributes to the plan adopted for strengthening feeble school children by proper medical means.

During this period of nine years there were in Antwerp 497 deaths from smallpox, only two of which were those of school children. They were children of seven and eight years, neither of whom had been revaccinated, and one had never been vaccinated. During this period there were, among an average annual school population of 13,506 children (subject to yearly renewals and changes), 53 cases of smallpox, none of which was among revaccinated children (Transactions of Tenth International Medical Congress at Berlin, vol. v., No. 15, p. 144).

DIAGRAM I.

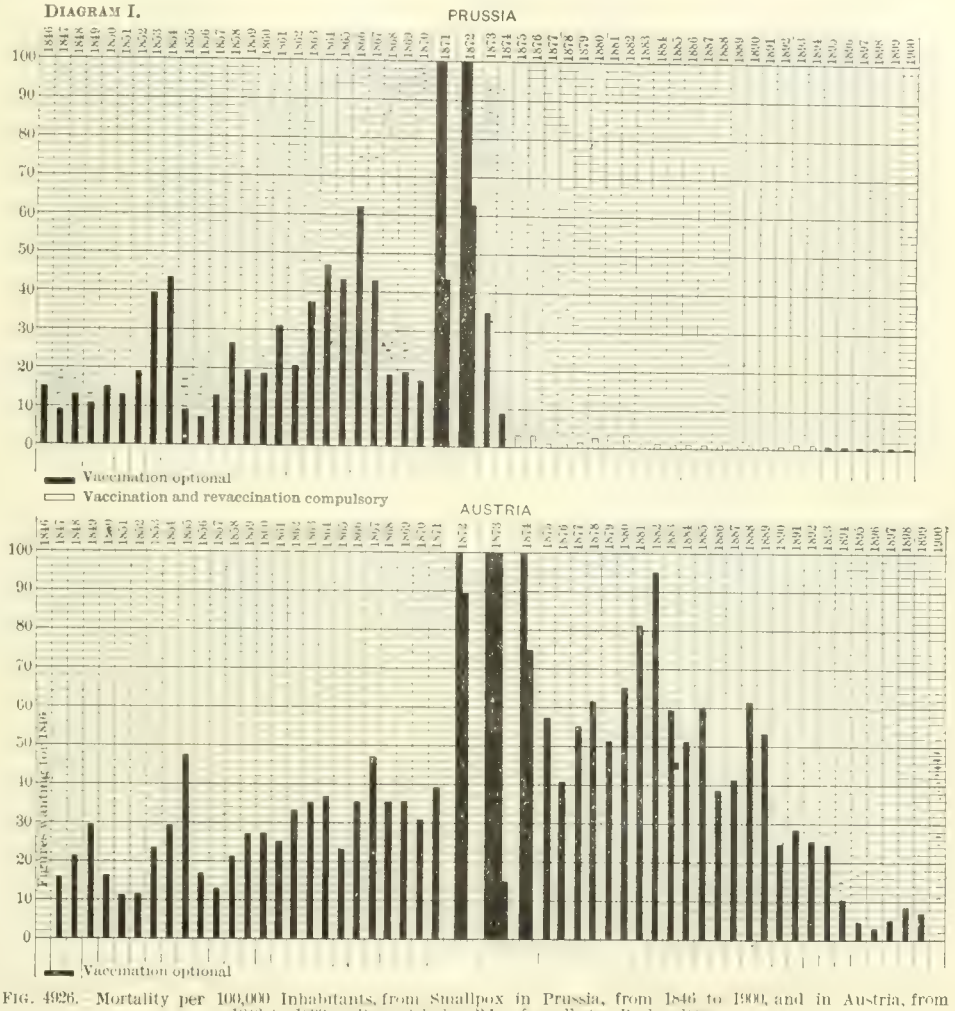

FIG. 4926.—Mortality per 100,000 Inhabitants, from Smallpox in Prussia, from 1846 to 1900, and in Austria, from 1846 to 1899. (From Schulz: "Impfung," etc., Berlin, 1888.)

The advantages of a system of compulsory vaccination and revaccination in protecting large communities from smallpox are clearly shown in the diagrams presented upon pages 127 and 128, copied from Schulz, "Impfung, Impfgeschäft und Impftechnik," Berlin, 1888, and reproduced in "Blattern und Schutzpockenimpfung," Berlin, 1896. The figures for completing these diagrams for the years since 1886 have been supplied from the official reports of the countries and cities represented.

Diagram I. presents the statistics of mortality from smallpox in Prussia and in Austria, showing the death rate per 100,000 from this cause in each country for a period of over fifty years, 1846 to 1900, in Prussia, and 1847 to 1899 in Austria. Vaccination was optional for the civil population in Austria for the whole period, while in Prussia it was compulsory after April 1st, 1875.

Diagrams II. and III. present the comparative mortality from smallpox of four German cities in which vaccination was compulsory after 1875, and that of four other large European cities in which it was either optional, or optional in the case of revaccination for the whole period (1861–1900), as it was in London.

The renowned statistician Körösi, of Budapest, has continued his valuable series of statistics. He contends that the ordinary comparisons of smallpox mortality in the periods before and after the introduction of vaccination, and the mortality from smallpox in countries and cities well or poorly vaccinated, do not constitute convincing proof of the value of vaccination. He entertained the idea that the proof could be sustained only when, in populous districts, the total number of the vaccinated and the unvaccinated is known, from which it would be easy to learn the mortality from smallpox among the vaccinated and the unvaccinated. But to obtain these figures from whole countries is not an easy task. The author's new method permits of a proof, in figures, of the influence of vaccination without a necessary knowledge of the number of the living vaccinated and unvaccinated. Until his inquiry was made, the vaccination question had been made to depend on the number sick or deceased from smallpox.

The tables which Körösi has published contain the number of persons treated for the most diverse diseases, and dying of the most diverse causes, their ages, and also whether vaccinated or unvaccinated. One table contains

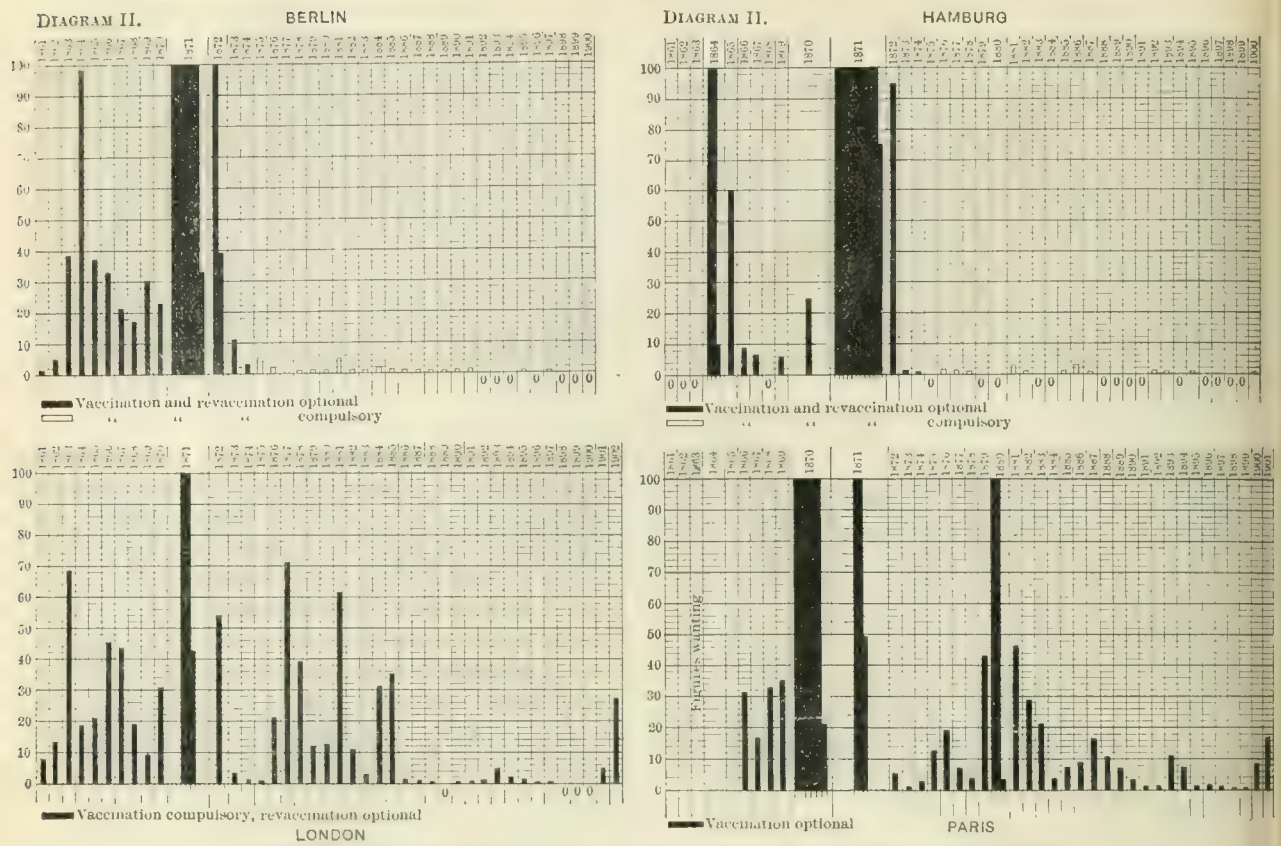

FIG. 4927.—Mortality from Smallpox in Several Large Cities per 100,000 Inhabitants. (From Schulz.)

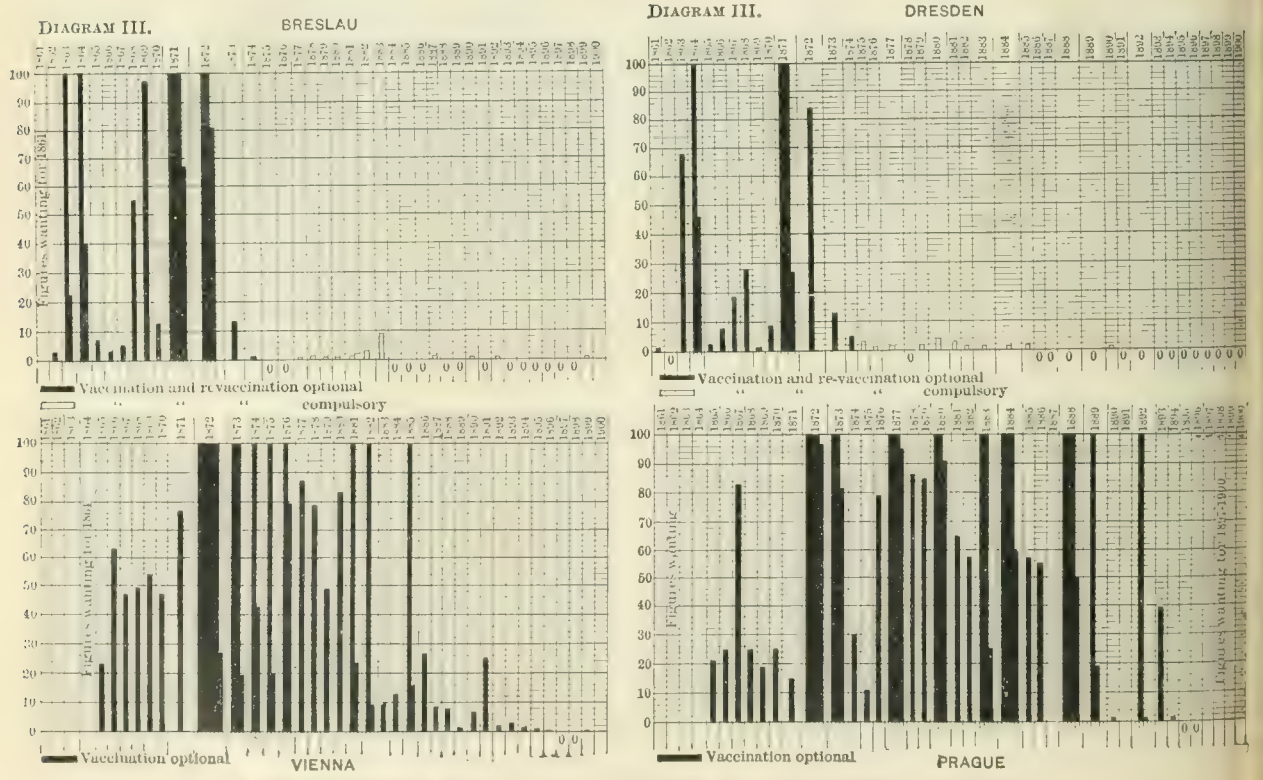

FIG. 4928. Mortality from Smallpox in Several Large Cities per 100,000 Inhabitants. (From Schulz.)

the condition as to vaccination of 53,320 persons treated in 1886, 1887, and 1888 in 19 Hungarian hospitals. The second table presents the statistics of 5,518 deaths in the same hospitals and for the same period. A third table gives the statistics of 58,639 deaths in 10 Hungarian cities for the same years, from different causes.

Of the persons sick with different diseases in the hospitals, 11.75 per cent. were unvaccinated. If vaccination had no effect upon smallpox *morbidity*, then the unvaccinated would have shared to the rate of about 11.75 per cent. in the contemporaneous 1,912 cases of smallpox. In other words, there would have been 225 cases of smallpox among the unvaccinated. Instead of this the number of cases of smallpox among the unvaccinated was 726. The neglect of vaccination, therefore, increased the liability to smallpox three and one-fourthfold. In the same manner the author concludes that the danger of death from smallpox is six times as great among the unvaccinated.

He also estimates that skin diseases destroy two persons out of every million, while by vaccination two thousand are saved.

A severe epidemic of smallpox broke out in Montreal, in 1885, principally in the last half of the year, and destroyed 3,164, out of a population of 167,501. In the report of the local board of health for that year these are classified as follows:

	Population.	Deaths from smallpox.	Ratio per 1,000 of the population.
French Canadians	93,641	2,887	30.8
Other Catholics	29,627	181	6.1
Protestants	44,233	96	2.1

This classification was a fair index of the condition of the population of Montreal at the breaking out of the epidemic, the French Canadians being chiefly the unvaccinated portion, and the remainder the vaccinated.

"In the years 1873 and 1874, there died in the East Indies about 500,000, and in 1875 and in 1876 about 200,000 people from smallpox. On the other hand, among the European troops in the same country (120,000), there were only two deaths from smallpox. The immunity of the troops was attributed solely to the thorough and rigorous enforcement of vaccination" (Wernher, p. 263).

The contested points in regard to vaccination may be reduced to three:

1. Whether, in an equal number of vaccinated and unvaccinated, fewer of the former are attacked by smallpox than of the latter (a question of morbidity).

2. Whether, in an equal number of vaccinated and unvaccinated, fewer of the former die of smallpox (a question of mortality). To the question as to the ratio of the deaths from smallpox to the number of those taken sick with the disease, Körösi applies the term lethality.

3. Whether or not vaccination is of itself innocuous, and whether or not other diseases may not be introduced by vaccination (Körösi: "Neue Beobachtungen über den Einfluss der Schutzpockenimpfung auf Morbidität und Mortalität").

In summing up his observations upon the influence of vaccination upon the population of Buda-Pesth, Körösi collected the data of 20,574 cases of illness in four hospitals in Buda-Pesth and fifteen provincial hospitals of Hungary, subsequent to April 1st, 1886.

Excluding 223 children under one year of age, because many are not vaccinated in their first year, he found that out of 18,572 persons sick with different diseases, *exclusive of smallpox*, 16,135 were vaccinated, and 2,437 were not vaccinated. Of the 16,135 vaccinated, 1,306 died, or 8.1 per cent.; of 2,437 unvaccinated, 321 died, or 13.2 per cent. So that the lethality of the unvaccinated was 60 per cent. greater than that of the vaccinated, the disease, smallpox in this instance, being excluded from the calculation.

With reference to the effect of vaccination on the mortality from smallpox, he found that there were treated in all 1,113 persons over one year of age ill with smallpox. Of these 631 were vaccinated, of which number 42 died, or 6.66 per cent.; 468 were not vaccinated, of which number 231 died, or 49.68 per cent.

There were 17 doubtful cases, of which number 3 died. So that, with reference to smallpox, the lethality of the unvaccinated was 800 per cent. greater than that of the vaccinated. Körösi admits fairly that not quite the whole of this difference can be attributed to neglect of vaccination, since from all other diseases upon which neglect of vaccination has no effect there died 160 unvaccinated to 100 vaccinated. Taking this into account, we may still predict that under like conditions the unvaccinated will have nearly a sixfold greater liability to death when stricken with smallpox than the vaccinated.

Dr. Buchanan, the medical officer of the Local Government Board, gives the following summary of death rates from smallpox among the vaccinated and the unvaccinated for the year ending May 29th, 1881:

Death rate of people of subjoined ages	Per million of each age of the vaccinated class.	Per million of each age of the unvaccinated class.
All ages	90	3,350
Under twenty years	61	4,520
Under five years	101/2	5,950

At the date of the British census of 1881 the number of children under ten years of age in London was 916,784, which was divided into about 55,000 unvaccinated and 861,000 vaccinated. In the same year the deaths from smallpox were as follows: 782 among the 55,000 unvaccinated, and 125 among the 861,000 vaccinated, or 1 in 70 of the former to 1 in 6,968 of the latter, a difference of nearly one hundredfold in favor of the vaccinated class.

The difference in these two methods of inquiry should be noticed, since Dr. Buchanan considers the effect of vaccination upon the population at large, while Körösi considers the effect of vaccination upon the mortality from smallpox as compared with the number of cases.

From all these observations, and from many more of the same character which might be quoted, we find that the *mortality among the unvaccinated* (without reference to the question of age distribution, or to the quality of the vaccination performed) *is from five to seven times as great as it is among the vaccinated.*

When, however, the conditions of the latter class are more carefully examined, it is found that *among vaccinated persons infected with smallpox* the danger of the disease is chiefly determined by the character or quality of the vaccination.

Mr. Marson, who first observed and made known the value of this principle, stated that, if the vaccinated are divided into two classes—(1) those who have been vaccinated in the best-known manner, and (2) those who have been badly vaccinated—the fatality from smallpox, if it infects the former, is but 5 per 1,000, and among the latter 150 per 1,000.

Classification of cases according to the character of vaccination.	Mortality rate in each class. Per cent.
1. Unvaccinated	35.00
2. Said to have been vaccinated, but having no cicatrix	24.56
3. Vaccinated:	
(a) Having one vaccine cicatrix	6.80
(b) Having two vaccine cicatrices	4.70
(c) Having three vaccine cicatrices	1.95
(d) Having four or more cicatrices	.55
(e) Having well-marked cicatrices	2.52
(f) Having badly marked cicatrices	8.82
4. Having previously had smallpox	19.00

Mr. Marson's observations further established the fact that the *degree of modifying power is in the exact ratio of*

the excellence and completeness of the vaccination as shown by the cicatrices. This principle was shown by observations upon 15,000 cases of smallpox which came under his observation in the course of thirty years.

The preceding well-known table is introduced in support of the statement.

From these observations it appears that the average of vaccinated persons, if they contract smallpox, have about one-sixth of the chance of dying from this disease which is incurred by those who have never been vaccinated; some of them, on account of the poor quality of the vaccination, incur one-third of that risk, while, on the other hand, others, thoroughly vaccinated, incur less than one-seventieth part of it. As to the prognosis of any case of smallpox, then, the question is not merely whether the patient has been vaccinated or not, but also *how* he has been vaccinated (Seaton, in "Reynolds' System," vol. i.).

In the examination of nearly a half-million children in England, with reference to the quality of the vaccination, the following causes of imperfection were noticed:

(1) The frequency with which practitioners, instead of attempting fully to infect the system, had been satisfied with insertions of lymph sufficient to produce only one, two, or three ordinary vesicles; (2) the want of due attention to the selection of the lymph used in vaccinating; (3) carelessness and clumsiness in the performance of the vaccination, so that, if the operation did not wholly fail, it very frequently resulted in a less degree of effect than it had been the aim of the operator to produce; and (4) the great and unnecessary extent to which the use of preserved and conveyed lymph was substituted for the vaccination with fresh lymph.

These observations were made upon children, most of whom had been vaccinated by public vaccinators, but a large number of whom had been vaccinated by private practitioners; and it was the impression of the observer that the latter were not so well vaccinated as the former. This observation has been substantiated by more recent inquiries (Report of the Local Government Board, 1884). This report, in commenting upon the variable quality of vaccination, and upon the inquiries of Dr. Stevens upon this subject, says: "The 125 children under ten years of age who died of smallpox after an alleged vaccination, must be reduced to 117 by deduction of those who were discovered, on his personal inquiry, not to have been vaccinated at all, or to have been 'unsuccessfully' vaccinated; and this number 117 divides into 82 vaccinated by private practitioners, and 35 by public vaccinators. Now, the number of vaccinated children under ten years of age, in London, is made up in about equal numbers of those vaccinated by private practitioners, and of those vaccinated at the public expense. Among the privately vaccinated there were 82 deaths, and among the publicly vaccinated there were but 35.

"From these figures we may deduce the fact that public vaccination in London protects against smallpox much more than private vaccination.

"Children privately vaccinated comprise most of the children of the upper classes, who certainly run less risk of smallpox infection than those of the poor. The comparatively large mortality among those privately vaccinated, therefore, becomes the more striking. And, undoubtedly, there are medical men to be found who, having formed some opinion of their own about the sufficiency of one vesicle, cannot be induced to set aside that opinion in deference to the indisputable evidence to the contrary that every smallpox hospital holds up to them."

In the Prussian army there has not been a single death from smallpox since 1874.

In Germany smallpox has diminished, since the enactment of the law of 1874, to a degree never before known, so far as records reach, while in the neighboring countries it prevails. It is for this reason that the German Government publishes an annual statement in which the condition of cities in neighboring countries in regard to smallpox is compared with those of Germany. The following table presents the figures of 1896 as published in the annual German report upon smallpox [10].

DEATHS FROM SMALLPOX, 1896.

	Number of inhabitants.	Deaths from smallpox in 1896.	Proportion per 1,000 inhabitants.
In the German Empire	52,612,568	10	0.02
In 265 German cities	14,125,027	2	.01
In 57 Austrian cities	3,619,109	64	1.77
In 15 greater cities of Switzerland	600,259	1	.17
In 70 Belgian cities	2,107,594	12	.57
In 108 greater cities of France	8,149,348	958	11.76
In 33 greater English cities	10,846,971	25	.23
In 12 greater cities of Holland	1,362,056	20	1.47

Under the title of "the balance of vaccination," Körösi discusses the advantage secured as contrasted with the infinitestimal dangers of the practice. He says: "There died in Buda-Pesth 153 children from skin diseases in six years, of which number 30 had been vaccinated. If the chances of death increased thirteen per cent. with the chances of disease, then instead of these 30 cases in the course of six years, there would have been 34 cases; accordingly 4 cases would have been charged to vaccination; in other words, for each year 4 to 6 cases, in a population of about 350,000, and for 100,000 inhabitants and one year, about one-fifth of a case. Therefore, in a city of one million inhabitants there would die, of skin diseases as a result of vaccination, at most two children more, while, on the other hand, 2,000 would be saved from the smallpox. The balance gives a gain of 1,998 lives. In whatever light the case may be considered, cowpox vaccination will continue to produce many hundred times more good than evil. So, although the great blessings of vaccination are not bought for nothing, still they are bought at a very trifling cost. And we may say boldly that vaccination is one of the grandest preservative forces for lowering mortality, and raising the average length of life." (This testimony comes from a layman, and one of the highest living authorities upon the interpretation of vital statistics.)

3. *The Effect of Vaccination upon the Age Distribution of the Mortality from Smallpox.*—Smallpox, when it occurs unmodified by vaccination, as in the eighteenth century, is essentially a disease of childhood; it might almost be said, of infancy. M. Marc d'Espine says of it: "The elective age of smallpox is childhood and infancy." Some of the names of this disease in different languages, which have come to us from ante-vaccination periods, are indicative of this characteristic, as Kinderpocken, Barnkopper, and possibly the English name smallpox, *i.e.*, pox of *the small*. It is as essentially a disease of children as scarlet fever or measles. In the latter disease a regular declining series is presented when successive ages are considered. For these diseases no method of prevention is known, and hence the statistics of mortality express unmodified natural affinities of such diseases for the earliest periods of life. For smallpox, since the introduction of vaccination, this declining series is interrupted in a most remarkable manner. The interruption is purely artificial, and is the expression of the effect of vaccination in postponing the greater mortality to a later period of life; and hence the necessity of revaccination, a subject which will receive further consideration.

The adjoining table expresses in four series of figures what may be taken as the expression (at least approximately) of the natural affinity of certain diseases. The population under five is a minority of the population (seldom more than fifteen per cent.), but it furnishes by far the majority of deaths from the diseases named—two-thirds of all deaths by scarlet fever, four-fifths of all deaths by unmodified smallpox, and a still greater proportion of deaths by measles and whooping-cough. In a word, these are all distinctively infantile diseases; and the obviousness of this fact represents three conditions: First, that the susceptibility to those diseases develops

itself very early in life; secondly, that the susceptibility, when once acted upon by its corresponding exterior cause, becomes exhausted more or less absolutely for the remainder of life; thirdly, that the exterior cause or infection has been of sufficiently frequent recurrence among the population for those relations of susceptibility to show themselves.

For the meaning of the diseases being infantile is, not that any insusceptibility to contract them is acquired in the mere act of growing up, but that, because the susceptibility develops itself at the commencement of life, and because the exterior influence which acts upon that susceptibility is seldom absent, therefore all who have outlived the first years of childhood have commonly had each susceptibility exhausted by suffering the disease to which it relates. Hence if all occurring cases of any such disease be classified according to the ages at which they happen, the resulting series of figures must necessarily have its maximum at that age when the special susceptibility is first fully developed. From this point it must undergo a more or less rapid and uninterrupted decline; the *uninterruptedness* being determined by the fact that at each succeeding age there will be fewer and fewer susceptible persons, the *rapidity* being graduated by the frequency or constancy with which the exterior cause is in operation.

PROPORTIONATE DISTRIBUTION BY AGE OF 1,000 DEATHS IN GENEVA BY SMALLPOX (1580-1760), BEFORE THE DISCOVERY OF VACCINATION, AND OF THE SAME NUMBER OF DEATHS BY WHOOPING-COUGH, MEASLES, AND SCARLET FEVER, AS OBSERVED IN 1847.

Ages.	Smallpox.	Whooping cough.	Measles.	Scarlet fever.
0- 1	202½	404½	155½	63¾
1- 2	191½	275	340¾	145
2- 3	190	138½	201½	171¼
3- 4	132¼	77¾	117	153
4- 5	88¾	47¼	68	123½
0- 5	805	943	883¾	656
5-10	155½	52½	91¾	254½
10-15	18¾	2¼	13½	54¼
15-25	13¾	¾	7	123¼
Above 25	7	1½	4	22½
At all ages	1,000	1,000	1,000	1,000

A report of the German Vaccination Commission shows that during the ten years following the enactment of its compulsory law of 1874, Germany not only had a smaller death rate from smallpox than ever before, but even passed from a position of inferiority to England to one of distinct superiority in regard to its immunity from smallpox. Smallpox mortality in the cities of Germany has become a trivial matter, while in London, Paris, and Vienna there have been quite appreciable epidemics, having their principal incidence upon the younger adult class of the population.

The following statistics as to the incidence of smallpox at certain ages are from the Report of the Medical Officer of the Local Government Board of England for 1884. While the 86 deaths among children under ten, stated in the column headed "Vaccinated community," contrast strongly with the 612 in the preceding column of the unvaccinated, there is no doubt, as the medical officer states, that even this number 86 is far too high, and is indicative of *sham* vaccination.

A comparison of the mortality from smallpox of children under one year of age living under the provisions of different laws, some of which are vigorously enforced, others optional or partially enforced, and also of populations entirely without vaccination, as was the case in the eighteenth century, is very instructive. Dr. Robertson, of Edinburgh, made such a comparison, and found that under the optional system in practice in Scotland from 1855 to 1864, the number of deaths from smallpox of children under six months of age was about equal to that of children whose ages were six to twelve months.

When vaccination became compulsory this ratio was greatly changed, and the number in the second six months was about one-fourth as large as that of the first six months. It was inferred that vaccination made the difference. A third fact, however, strengthened this inference, and that was the ratio existing before vaccination was known. This was to be found in the carefully kept statistics of the Kilmarnock register already quoted.

RATIO OF DEATHS FROM SMALLPOX BETWEEN SIX AND TWELVE MONTHS OF AGE, TO ONE HUNDRED DEATHS FROM SMALLPOX UNDER SIX MONTHS, IN THREE SELECTED PERIODS.

Age.	1728-1763. Kilmarnock. Vaccination unknown.	1855-1864. Scotland. Vaccination optional.	1865-1879. Scotland. Vaccination compulsory.
Under 6 months	100	100	100
From 6 to 12 months	491	103	26

The first ratio may be taken as the normal one of natural smallpox. It is a disease nearly five times as fatal in the second as in the first six months of life. But when modified by optional vaccination in the second six months, the mortality is reduced from 491 to 103. And when vaccination becomes compulsory, as in the third period, the 103 is further reduced to 26.

The question may be asked, How far is this decrease in smallpox mortality to be attributed to causes other than vaccination? Improved hygiene and treatment may have exercised considerable effect upon the mortality, but they can have but little bearing upon the facts quoted in the last table. Such an enormous improvement, at the rate of nearly 20 to 1, could never have been due to mere measures of sanitation. Let the following table of the rate of improvement of certain infectious diseases illustrate this:

RATE PER ONE THOUSAND PER YEAR OF DEATHS FROM CERTAIN INFECTIOUS DISEASES IN KILMARNOCK IN 1728-64, AND IN ENGLAND AND WALES IN DIFFERENT PERIODS.

Disease.	Rate in Kilmarnock. 1728-64.	Rate in England.	Rate of decrease.
Measles	0.615	(1861-71) 0.4399	100 to 70
Whooping-cough	.7671	" .5273	100 to 68
Fever (including scarlatina	3.4722	" 1.8474	100 to 53
Smallpox	4.1071	(1854-79) .208	100 to 5

Deaths from smallpox have therefore decreased 14 times more than those from measles, 13 times more than those from whooping-cough, and 10 times more than those from fever.

From the instructive comparison given by Dr. Vail, the following conclusions are drawn:

1. Smallpox was epidemic every four and one-quarter years (1728-64).

2. Its death rate per 1,000 per year was nearly 20 times as great as it now is. 3. Its death rate under five years of age was 35 times as great as it now is.

4. The mean age at death from smallpox was two and one-half years in the last century, and is now nearly twenty years.

5. The death rate from smallpox in the second half-year of life is now only a fourth of that in the first half-year, while formerly in the second half-year it was nearly 5 times as great as in the first half-year. 6. The smallpox death rate has improved about 12 times as fast as the death rate from measles, whooping-cough, and fever.

The fact that smallpox when allowed to pursue its natural course, unmodified by vaccination, is essentially a disease of childhood, is illustrated in a most forcible manner in the sketch of smallpox in Kilmarnock in the last century, already quoted.

Of the 622 persons who died of smallpox in that town between 1728 and 1764, 586, or 94.2 per cent., were five years of age and under. Seven only were over ten years of age, and the oldest was but twenty-six.

In the different epidemics which fell upon that community, the time from the height of the first epidemic to that of the second was but four years and eight months, and of the 45 children who succumbed in 1733, 44 were less than four years and eight months of age, the remaining one being seven years of age. Thus only one child that died in the epidemic of 1733, had been alive previous to the height of that of 1728. The disease had to secure its victims almost wholly from the population that had come into existence since its last visitation. One epidemic left almost no victims for its successors; in the same way, hardly any had been left to it by its predecessors. It called at every door, and nearly all who were not disease-proof came within its grasp.

Epidemic years.	Interval since height of former epidemic.	Total deaths, smallpox.	Deaths of children born since height of former epidemic.	Deaths among children who had passed safely through one epidemic.	Deaths among persons who had passed through more than one epidemic.
1728–29	Unknown	66			
1733	4 years 5 months.	45	44	1	
1736	3 years 5 months.	66	58	7	1
1740	3 years 7 months.	66	60	5	1
1744–45	4 years 8 months.	74	67	6	1
1749–50	5 years	84	79	4	1
1754	4 years 6 months.	95	84	11	
1757–58	3 years 2 months.	45	39	6	
1762	4 years 8 months.	66	53	11	2
Cases occurring between epidemics.		14	8	5	1
Total		621	492	56	7
Percentage			88.6	10.00	1.2

The principal point shown in this table is that, on an average, over eighty-eight per cent. of those who died in one epidemic had been born since the previous one; that ten per cent. who died had passed safely through one epidemic; and that only one per cent. had lived through more than one outbreak.

The next table shows that these epidemics, to nearly nine-tenths of their extent, did not practically occur in a

Section of Population Born since Former Epidemic.

Height of epidemic.	Born since height of former epidemic.	Died of various diseases, excluding smallpox.	Remaining to form a field for new epidemic.
May, 1733	614	90	524
October, 1736	476	82	394
May, 1740	501	89	412
January, 1745	506	68	438
January, 1750	634	107	527
July, 1754	648	131	517
September, 1757	445	41	404
May, 1762	690	110	580
Totals	4,514	718	3,796
Averages	564	89	475

population of 4,200, but in a population of 475 people. And the average number of deaths in this population was 60, or at the very high rate of 126 per 1,000 living in each epidemic year. Now the number of attacks in unvaccinated children under five years of age is two for every death. As many die as recover. Therefore, of every 100 children born in Kilmarnock, no less than 25 were seized with smallpox at the very first epidemic after their birth.

"These two tables show that, as regards smallpox, there were, in fact, three Kilmarnocks. One, a Kilmarnock of 3,700 persons, had no fear of its attacks. These had already met and battled with the disease fiend. On many were to be seen the marks of the conflict. Some were blind, some had lost their hearing, many were permanently injured in constitution, and very many were scarred and disfigured for life; and, for every one that conquered, another had fallen, never to rise again. There was indeed a second Kilmarnock under the green sod of the kirkyard. The Kilmarnock which had reason to dread the epidemic's approach was a Kilmarnock the least able to meet it. It consisted of a band of little children, numbering less than five hundred in all. Every such group that came into existence had to face, within four or five years of its birth, the most terrible physical enemy that it would ever meet; and, having fought the battle, some were added to the maimed and distorted who formed so large a portion of the population, and others were laid beside those who had been destroyed by former epidemics. One can barely imagine what must have been the feelings of a mother regarding these fearful visitations. Even where the town was free from the pestilence, there would be the constant foreboding of its all too certain coming; and when at last the first case occurred—when the doctor was called in, and pronounced the disease to be the dreaded pox—his words would be heard as a sentence of death to some member of almost every family containing little ones; and, as the news spread from house to house, with what a despairing clutch would each mother press her darling to her breast, and beg Almighty God to command the destroying angel to pass by her door! After the lapse of a hundred and fifty years, one can have little conception of the real meaning of a smallpox epidemic. But the old parish register has enabled us to apprehend something of its horror, and I venture to say that, if the antivaccinationists had their will, we would ere many years be again experiencing somewhat of the awful visitations which were so familiar in old Kilmarnock."

The following figures and diagrams show in a conclusive manner the fact that smallpox in the eighteenth century was beyond question a disease almost exclusively of young children. They also show in quite as conclusive a manner the modifying effect which vaccination has had upon the age incidence of smallpox mortality.

The figures for the smallpox diagram (eighteenth century) were made from an average of the records of several English and continental towns which are given in the foregoing pages. This average was as follows: Out of each 1,000 deaths from smallpox 805.5 were those of children under five years, 155.5 were those of children from five to ten years old, 26.5 from ten to twenty years, 10 from twenty to thirty years, 2.5 from thirty to forty years, and 25 over forty years. (See lower left-hand diagram in Fig. 4929. In these four diagrams the inci-

Contribution of Various Ages to One Thousand Smallpox Deaths of all Ages.

Ages at Death.	Geneva, 1580–1760.	Kilmarnock, 1728–1764.	Pudsey, 1771–1813.	Chester, 1774.	Stockholm, 1774–1800.	London, 1848–1851.	Paris, 1842–1851.	London, 1884.		
								Unvaccinated community.	Vaccinated community.	Total inhabitants.
0–10	961	988	982	1,000	961	815	397	612	86	343
10–20	26½	5	17	....	31	59	133	146	173	170
20–30	10	7	1	....	....	83	329	108	319	213
30–40	....	....	....	....	8	32	110	72	221	142
40 and upward.	2½	....	....	....	....	11	31	62	201	132
Totals	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000

dence of disease is measured by the horizontal length of the shaded portions, not by their area, since the age-periods from birth to twenty years are five years each, while the remaining periods are ten years each.)

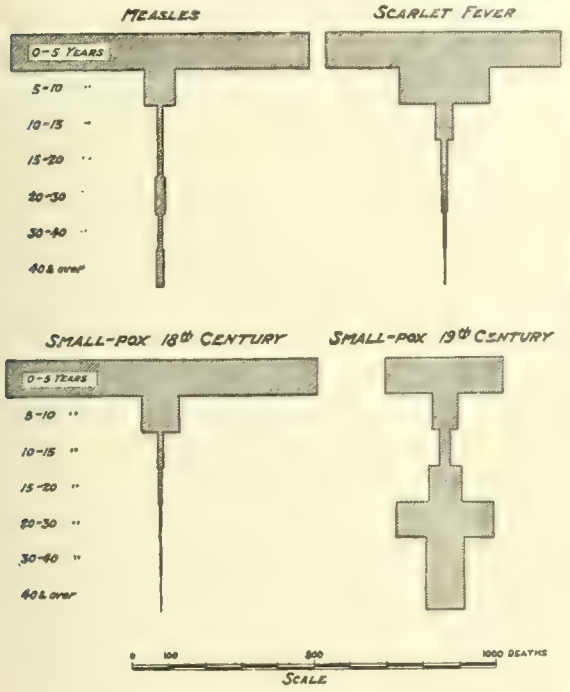

FIG. 4929.—Distribution of 1,000 Deaths From Certain Causes by Ages.

The figures for Massachusetts, 1863–1900, also show conclusively the cutting down of the smallpox death rate of infants and the increase in that of young adults (twenty to thirty years) in consequence of neglect of revaccination at the proper period.

MASSACHUSETTS.—DISTRIBUTION OF 1,000 DEATHS FROM SMALLPOX, MEASLES, AND SCARLET FEVER, FOR THIRTY-EIGHT YEARS, 1863–1900.

Ages.	Smallpox.	Measles.	Scarlet fever.
0–5 years	326.6	826.7	656.7
5–10 years	70.6	81.1	250.5
10–15 years	33.4	16.5	50.5
15–20 years	86.4	16.5	17.9
20–30 years	270.0	27.1	15.9
30–40 years	106.1	11.7	5.6
40–50 years	44.7	7.2	1.2
50–60 years	30.4	3.9	1.0
60–70 years	17.3	3.5	.5
Over 70 years	14.5	5.8	.2
	1,000.0	1,000.0	1,000.0

The following figures show the death rates per 100,000 living at each age-period from smallpox in a population in which vaccination is moderately enforced. They include the statistics of about 3,500 deaths from smallpox which occurred in Massachusetts in the thirty-eight years, 1863–1900.

DEATHS FROM SMALLPOX IN EACH YEAR OUT OF 100,000 LIVING AT EACH AGE PERIOD. MASSACHUSETTS.

Under 5 years	15.0	40–50 years	1.8
5–10 years	3.3	50–60 years	1.8
10–15 years	1.7	60–70 years	1.6
15–20 years	4.2	70–80 years	1.7
20–30 years	6.1	Over 80 years	3.5
30–40 years	3.1		

Dr. Tissot, writing about the middle of the eighteenth century, said of smallpox:

"Smallpox is the most frequent, the most extensive of all diseases. Out of 100 persons there are not more than 4 or 5 exempted from it. *People generally take the ... pox in their infancy or in their childhood.*" (Advice to the People with Respect to their Health," 1762, p. 156.)

The Duration of the Protective Power of Vaccination.—Gerstäcker, as quoted by Wolffberg, states (*Centralblatt für allg. Gesundh.*, 1888, p. 182) that the cardinal principle of the duration and efficiency of the protection afforded by vaccination depends essentially upon the intensity of the preceding vaccination, and upon those changes which—independent of every attempt at protection—the natural individual predisposition to smallpox undergoes in the course of life, although reduced to a definite lower standard by vaccination.

The Comparative Protection Afforded by Vaccination and by Smallpox.—Both Marson and Simon expressed the opinion, before the Parliamentary Committee of 1871, that the protection afforded by an attack of smallpox against a subsequent attack was greater than that afforded by vaccination (Replies 3,517–3,521; 4,220–4,224).

In the early years of vaccination it was quite a common practice to expose vaccinated people to the smallpox either by contact or by inoculation, for the purpose of testing the efficacy of the practice. The town of Milton, Mass., in September, 1809, voted to test the question upon twelve children who had been vaccinated in July of the same year. Twelve vaccinated children were therefore selected and inoculated with smallpox lymph. They were quarantined during fifteen days at a hospital provided for the purpose, and the following certificate was issued on their release:

MILTON, October 25th, 1809.

The twelve children whose names are written on the back of this card were vaccinated at the town inoculation in July last; they were tested by smallpox inoculation on the 10th instant, and discharged this day from the hospital, after offering to the world, in the presence of most respectable witnesses, who honored Milton with their attendance on that occasion, an additional evidence of the never-failing power of that mild preventive, the cowpox, against smallpox infection; a blessing great as it is singular in its kind, whereby the hearts of men should be elevated in praise to the Almighty Giver.

AMOS HOLBROOK, *Physician.*
OLIVER HOUGHTON, *Chairman of the Committee for Vaccination*

[Card in possession of Massachusetts State Board of Health.]

As compared with the earlier practice of inoculation with smallpox lymph, vaccination has the great advantage over the latter that its protection is afforded without risk to life, without disfiguring the features, without causing loss of sight or of hearing, and without the risk of propagating a highly infectious, loathsome, and deadly disease among the community.

BOVINE VACCINATION.—The term bovine, or animal, vaccination is applied to that which is practised by the aid of vaccine lymph cultivated in bovine animals. Warlomont very truly says that the term *animal vaccination* is purely conventional; the vaccine lymph from an infant is just as much an animal product as is that from a heifer.

With reference to the origin of the practice, Dr. Warlomont states that an aged physician had, in his youth, seen his father, the village doctor, inoculate the teats of a cow with human vaccine, preserved through the winter in order to renew the stock of fresh lymph at the commencement of each vaccinating season. Such was a common practice, and it has been carried out for years in Germany, and especially in Bavaria. This method of practice has been called retrovaccination. It has also been practised to a considerable extent in the United States. Supplies of vaccine virus were largely obtained for use in the army by this method during the latter part of the Civil War (1861–65), and while this method has been vehemently opposed by some, it is also true that no evidence has been adduced to show that such vaccination, when properly transmitted from a healthy infant to the heifer, and thence, after one or more successive transmissions from animal to animal, is again transmitted to the human species, is less protective against smallpox

than that which has never been cultivated upon other soil than that of the cow. The German Government takes this ground and sanctions its employment in its instructions upon this subject.

That method to which is now given the term animal or bovine vaccination is of later origin, and also has a more restricted application. Warlomont defines animal vaccination as "the product of natural horsepox or cowpox which has been cultivated upon heifers," and has never quitted that place (or medium) of cultivation ("n'ayant jamais quitté ce lieu de culture"). This method was practised in a limited degree as early as 1800, by Duquenelle, at Rheims, and by Valentine, at Nancy. It was introduced into Naples in 1810 by Galbiati, and continued by his pupil, Negri. Both of these early experimenters occasionally resorted to retrovaccination, but Negri finally began a series of continuous vaccinations, for which he obtained his original supplies, on two different occasions, from animals found to be affected with natural cowpox.

In 1864 M. Lanoix, a French physician, visited Naples to study this method of vaccination, and thence introduced the practice into Paris in the same year. A commission was appointed by the Government in 1866, whose report favored the practice of animal vaccination, and the first virus employed by them was that which had been obtained from Naples. A new source was soon found at Beaugency, in France, in 1866, and still later another at St. Mandé, near Paris. Other cases of natural cowpox may be found detailed in an article in the *Revue d'Hygiène* (July, 1888) by Dr. A. Layet, entitled "Les Sources naturelles du Vaccin." Dr. Seaton, in his report on animal vaccination to the Local Government Board of England, made after a visit to Paris and other parts of the Continent in 1869, states that Drs. Lanoix and Chambon, who had introduced animal vaccination into Paris, "saw no advantage in keeping these *two lymphs* distinct, and the virus which they have employed since 1866 is a mixture of the two natural sources discovered at Beaugency and at St. Mandé."

Dr. Seaton had made an unfavorable report upon Bovine Vaccination, urging, in the *first* place, the difficulty of transmitting the virus from one animal to another successively; *second*, the great risk of failure in transmitting it from the calf to the human subject; *third*, the inferior preservative quality of bovine lymph.

In reply to this it may be said:

First. With reference to the facility of infecting calves or heifers continuously with vaccine lymph, Dr. Cory states, in his report to the Local Government Board in 1886, that 153 calves were vaccinated with lymph of one hundred and twenty hours' growth, and all of them proved susceptible to vaccination; 8,600 insertions were made, resulting in 8,242 vesicles (an insertion success rate of 95.8 per cent.); 94 calves were vaccinated with lymph of ninety-six hours' growth, producing 5,440 vesicles out of 5,631 insertions (an insertion success rate of 96.6 per cent.); 3 other calves were vaccinated with lymph of one hundred and sixty hours' growth in 144 places, producing 142 vesicles.

In the writer's experience not more than five per cent. of bovine animals of different ages prove refractory to vaccination, and the operation of transmitting the vaccine infection successfully from animal to animal is not, in the hands of an expert, attended with difficulty. The reasons for the comparative insusceptibility of adult animals are given elsewhere.

Second. As to the transmission of the infection from the bovine animal to the human subject (under like conditions as to the quality and freshness of the lymph used), the operation is quite as successful as with humanized lymph, and by some authorities the percentages of success are reputed as greater than with humanized lymph.

In Illinois, in 1882, out of 138,488 primary vaccinations with bovine lymph, 82.7 per cent. were typical, and out of 15,448 performed with humanized lymph, 76.9 per cent. were typical. Dr. Cory vaccinated 4,688 persons, and of these 4,212 were successful in five places, 238 in four places, 92 in three places, 51 in two, 37 in one, and 17 were unsuccessful in the first trial. Excluding a very few who did not return for inspection, Dr. Cory's insertion success rate was 96.5 per cent., Mr. Murphy's 99.9, Mr. Stott's 90.6.

Dr. Pissin, of Berlin, in 1882, reported that he had made 12,679 vaccinations from 18 calves, with a ratio of success of 98.1 per cent. in primary vaccinations, and 91.3 per cent. in revaccinations, using scarifications only. Pfeiffer, of Weimar, obtained a success of 98.6 per cent.; Rissel, 97.8 per cent.; Reissner, 98.6 per cent., and Voigt, 99.4 per cent.

At the Hamburg vaccine establishment the ratios of reported success were as follows: In 1878, 69 per cent.; in 1879, 82 per cent.; in 1880, 73 per cent.; in 1881, 82 per cent.; in 1882, 85.4 per cent.

Weiler, on the contrary, found the humanized lymph to give better results, obtaining 97.3 per cent. in primary vaccinations with humanized lymph, and 86.8 per cent. with bovine lymph.

Third. As to the preservation of animal lymph as compared with that of humanized lymph.

1. As to its use upon calves. Dr. Cory, in the report already alluded to, made careful observations as to the preservation of lymph stored in tubes, and established the possibility of such preservation for a period of two years. His results were as follows: The lymph referred to in these observations was partly of ninety-six and partly of one hundred and twenty hours' growth, none being taken later than one hundred and twenty hours after insertion. He also states that lymph taken at a later period deteriorates more rapidly, and is apt to produce spurious results, just as happens occasionally with humanized lymph taken at a later date than the eighth day.

Number of days during which lymph was preserved in tubes before using.	Number of insertions with it on calves.	Successful insertions on calves.	Insertion success rate per cent.
2	3,998	3,380	84.7
4	1,438	1,139	74.2
6 to 8	255	184	72.1
9	431	309	71.6
11 to 12	337	273	70.6
14	263	214	81.3
16	288	207	71.9
17 to 46	639	472	73.8
53 to 93	445	332	74.6
100 to 200	388	258	66.5
201 to 500	104	17	16.3
500 to 600	135	45	33.3
600 to 700	82	24	35.0
816 to 858	72	4	5.5

2. As to its use upon the human subject. Like the former, this lymph was also of one hundred and twenty and of ninety-six hours' growth, in about equal proportions. A part was stored in tubes and a part upon ivory points, in regard to which Dr. Cory says that within four months of storage there is an advantage in points over tubes as a method of storage, and a period of one hundred and fifty-four days appears to be the longest interval that should be allowed to elapse between the taking of calf lymph on points and its use on children. For longer periods the lymph in tubes retained its powers better than that preserved upon points.

The three tables on the opposite page were the results of Dr. Cory's observations on this point.

From Italy and from France the practice of bovine vaccination extended to other countries. In February, 1865, it was introduced into Brussels by Dr. Warlomont, who employed successively lymph from the Neapolitan source, afterward from the Beaugency source, and finally from a third source obtained at Esneux. A state vaccinal institute was finally established at Brussels under his charge, where the practice of bovine vaccination has

RESULTS OF VACCINATION WITH CALF LYMPH, PRESERVED ON POINTS AND IN TUBES, FOR VARIOUS PERIODS.

Mode of Storage.	Time during which lymph was stored.	Aggregate number of insertions made (five to each child).	Aggregate number of successful insertions.	Percentage of insertion success.
Points.	Under 10 days	40	34	85
	10 to 20 days	25	21	84
	20 to 50 days	70	63	90
	50 to 100 days	70	51	73
	100 to 154 days	60	29	48
	Over 154 days	30		
Tubes.	Under 10 days	75	65	87
	10 to 20 days	25	17	68
	20 to 50 days	65	45	69
	50 to 100 days	45	30	67
	100 to 154 days	20	17	85
	150 to 280 days	40	33	82

COMPARATIVE RESULTS OF PRIMARY VACCINATIONS WITH HUMANIZED AND BOVINE VACCINE VIRUS IN ILLINOIS (1881–82).

	Totals.	Results.		
		Typical.	Modified.	Poor.
Bovine virus	138,488	114,605	12,295	11,588
Percentages		82.7	8.9	8.4
Humanized virus	15,448	11,893	2,275	1,280
Percentages		76.9	14.8	8.3
Totals	153,936	126,498	14,570	12,868
Percentages		82.2	9.5	8.3

COMPARATIVE RESULTS OF REVACCINATIONS WITH HUMANIZED AND BOVINE VIRUS, ILLINOIS (1881–82).

	Totals.	Results.		
		Typical.	Modified.	Poor.
Bovine virus	76,154	45,187	14,010	16,957
Percentages		59.3	18.4	22.3
Humanized virus	3,250	2,206	450	614
Percentages		67.9	13.2	18.9
Totals	79,404	47,393	14,440	17,571
Percentages		59.6	18.2	22.2

Per cent. of vaccinations with bovine virus 79.2
Per cent. of vaccinations with humanized virus 20.8

been carried out with the greatest care, for the gratuitous distribution of lymph both of humanized and of bovine stock. The institute was established on condition that both sorts of lymph should be distributed from it. Dr. Warlomont, by the thorough character of his work as well as by his published writings upon the subject, has accomplished very much toward the general introduction of bovine vaccination.

Bovine vaccination was introduced into Berlin in 1865 by M. Pissin, and is still conducted there, and also at Vienna; the amount of bovine lymph used, as compared with the humanized, having increased rapidly from year to year since its introduction. Establishments for the production of animal lymph are now in operation at Berlin, Halle, Kiel, Kassel, Munich, Nuremberg, Dresden, Bautzen, Leipsic, Frankenberg, Stuttgart, Cannstadt, Karlsruhe, Darmstadt, Schwerin, Weimar, Bamberg, Lubeck, Hamburg, Bremen, Strassburg, and Metz. This practice has gradually made its way into other countries of Europe, and now nearly every large city has its vaccine institute or establishment for the propagation of bovine lymph. It is also in use under the auspices of the British Government in India. It was introduced into Bombay in 1881, and into Madras and Bengal in 1882, and was introduced into Japan in 1874.

The following table illustrates the rapidity with which bovine lymph has taken the place of humanized lymph in Germany since 1879:

PERCENTAGE OF BOVINE LYMPH IN USE IN GERMANY, 1879–1900.

	Per cent.		Per cent.
1879	2.6	1890	89.1
1880	3.3	1891	96.8
1881	4.0	1892	98.5
1882	7.1	1893	98.9
1883	11.2	1894	98.9
1884	19.1	1895	99.87
1885	33.1	1896	99.88
1886	54.2	1897	99.96
1887	68.4	1898	99.96
1888		1899	99.72
1889	77.4	1900	99.94

The foregoing figures for the years 1879–87 are from the "Arbeiten aus dem Kais. Gesundheitsamte" and for the years 1889–1900 from the "Mittheilungen."

England was slow to adopt the new method of vaccination; Dr. Seaton's unfavorable report in 1869 undoubtedly delayed its introduction. This report, however, contained much valuable information upon the subject, which led to its careful consideration, and finally to its introduction under the direction of the Local Government Board in 1881, the use of either humanized or bovine lymph being optional. The experiments of Dr. Cory, establishing the possibility of the transmission of syphilis by humanized virus, even under the most rigorous conditions, undoubtedly strengthened the position of the board in introducing the bovine virus.

"As the result, however, of the findings of the Royal Commission on Vaccination," says Dr. Copeman,[12] "legislative measures have now been introduced by which arm-to-arm vaccination will be entirely superseded, in public work at any rate, by animal vaccination, and the adoption of the use of preserved glycerinated calf lymph having been determined on, the necessity for stational attendance will disappear, except in so far as may appear desirable for purposes of control, or in order to provide facilities for teaching."

By the term "stational attendance" the writer refers to certain definite places and times, when and where facilities were provided for the work of arm-to-arm vaccination from healthy infants. Opportunities for vaccination upon the old arm-to-arm method were usually furnished weekly in the large cities, and about once in three months in the country districts.

In the United States bovine vaccination had been attempted on various occasions previous to its more general introduction in 1870–71. Dr. John Yale, of Ware, Mass., writes to me that in 1855, his cow "had the cowpox, a single umbilicated vesicle on the udder adjoining the teat; I took the crust, and vaccinated with it, used the matter upon calves, and so kept up a supply for years." He also stated that in 1844 he had observed cowpox in a herd of thirty cows belonging to Mr. Truman Curtis, of Torringford, Conn. The milkmaids and some of the men servants contracted vaccinia upon their hands from this herd.

In March, 1865, Dr. E. Cutter, of Woburn, Mass., detected kinepox in at least two instances in the town of Lexington, where the disease was more or less prevalent, and at times very troublesome at dairy farms. From two of these cases he vaccinated two cows, and obtained a succession of lymph, which was used to a considerable extent in the vaccination of soldiers in the Army of the Potomac, in the spring of 1865. A report was made upon these cases by Surgeon J. J. Milhau, U. S. A. (dated March 29th, 1865), who visited and personally inspected twelve of the animals thus vaccinated ("Medical and Surgical History of the War of the Rebellion," Medical Volume, part iii.).

Previous to the date referred to (March, 1865) Dr. Cutter, as stated in his report of 1872, had employed retrovaccination quite largely, and with excellent success, and in this respect had followed very much the same method which had formerly been employed by Negri, at Naples.

In 1870 Dr. Henry A. Martin, of Roxbury, Mass., imported lymph of French origin, and organized a well-equipped vaccine establishment at which a constant succession of heifers has been vaccinated since that time, the work having been continued after his death by his

sons. To him the work of successfully bringing bovine vaccination to popular notice in the United States, as a substitute for humanized vaccination, was largely due. Dr. Martin also obtained lymph from cases observed in

by contagion, such as syphilis, does not convey such germs, in any case, and gives rise only to vaccinia."

The question was again fully discussed in 1864, by the same body, and it was finally admitted by the Academy

Fig. 4630 Vaccinating a Calf. (By permission of the H. K. Mulford Company.)

the neighborhood of Boston, which was also successfully transmitted to a succession of heifers. Others soon followed him in different parts of the United States, especially Dr. Frank P. Foster, of New York, and Dr. E. L. Griffin, of Fond Du Lac, in Wisconsin.

The production of vaccine material in the United States is now (1903) mainly in the hands of a few private producers, who furnish most of the vaccine lymph used in the country. The principal producers are the H. K. Mulford Company, of Philadelphia, Parke, Davis & Co. of Detroit, Mich., and the National Vaccine Company of Washington. All of these are equipped with establishments of ample size, furnished with modern appliances, including excellent bacteriological laboratories and capable of producing vaccine material ample in quantity and reliable in quality for general use. Considerable quantities are also exported abroad for use in other countries.

At present it is safe to say that practically all of the lymph used for vaccination in the United States is of direct bovine origin—produced by artificial propagation.

There are certain advantages in the employment of animal lymph which may be detailed as follows:

The avoidance of the transmission of certain diseases common to mankind, which it has been conclusively proven may be transmitted by the process of vaccination; for while it is undoubtedly true that millions are annually vaccinated without the occurrence of a single case of such transmission, it is also true that a sufficient number of cases are on record to establish the possibility of such transmission.

The French Academy of Medicine had, as long ago as 1830, proclaimed, almost in dogmatic terms: "Vaccinate without fear, for the vaccine virus taken from subjects afflicted with complaints susceptible of communication that vaccinal syphilis was an incontestable fact, and while it was of very rare occurrence its possibility could not be doubted. Ricord said of it: "I at first denied the possibility of the transmission of syphilis by vaccination, but facts repeating themselves, and becoming more and more confirmatory, I admitted with reserve, and even with repugnance this mode of transmission. To-day I do not hesitate to state it as a fact."

Proofs of the occurrence of vaccinal syphilis are to be found in the writings of Depaul, of Viennois, and others, where about three hundred cases are given in detail. The reported cases are mainly of French and Italian origin, those detailed by Professor Cerioli and the Rivalta cases constituting a large part of the number. While the earlier English writers have been slow to accept the possibility of such transmission, some recent experiments have apparently settled the question conclusively that the danger exists, so far as vaccination with humanized lymph is concerned, although the transmission is of extremely rare occurrence.

It is certain that hundreds of thousands of vaccinations were made every year without the occurrence of the accident in question, and hundreds of busy practitioners passed through the period of active practice, during which they were called upon to make frequent vaccinations, without meeting a single case.

Three methods have been detailed as possible for the occurrence of vaccinal syphilis:

(1) By the mixture of vaccine lymph with the products of a syphilitic skin eruption.

(2) By mixture with the blood of a syphilitic person.

(3) By the use of the clear lymph of a vaccine vesicle existing on the person of a syphilitic.

With reference to the question of the transmission of

syphilis by inoculating the blood of a syphilitic upon a healthy person, there can be but little question. The question has been proven, both by observation and by experiment.

With reference to the transmission of syphilis through the medium of the clear vaccine lymph containing no blood, the experiments of Dr. R. Cory, an officer of the Local Government Board of England, established the possibility of such communication. These experiments were witnessed by a committee of experts comprising the noted surgeon, Jonathan Hutchinson, together with Drs. Bristowe, Humphrey, and Ballard (see Twelfth Report of Medical Officer of the Local Government Board of England, p. 46).

Since the introduction of animal vaccination generally into different countries, the reports of such cases have become comparatively rare, and consequently the discussion of this question has now lost much of its practical importance.

When it is remembered that at least five hundred millions of persons have undoubtedly been vaccinated since the introduction of vaccination by Jenner, the ratio of these cases of transmitted syphilis to the whole number is surprisingly small.

Another reason for the use of bovine virus lies in the facility with which an abundant supply of lymph may thus be secured for use at short notice. The occasional advent of smallpox among the crowded populations of large cities renders the production of large quantities of vaccine lymph in a brief space of time an absolute necessity.

The amount of vaccine lymph which may be obtained from one animal, as compared with the paucity of material which it is practicable to obtain from a healthy infant, is very large.

From two thousand to ten thousand charges of effective lymph upon ivory points is not an unusual quantity to be taken from a single heifer, and nearly equal quantities can be procured under modern methods in which the vaccine material is finally mixed with glycerin. It is, therefore, a decided advantage to be able to resort to the cow, and thus to avoid the objections which may be raised against the taking of supplies of lymph from infants. It is especially desirable, when lymph is supplied by the authorities of state and city governments, that such lymph should be of the best quality. Such authorities are under moral obligation to furnish to the people a vaccine lymph which is beyond all suspicion in the matter of freedom from contamination of disease.

These two faults, the possibility of contamination with syphilis and the relative paucity of lymph, were especially the faults of the Jennerian method of vaccination —and in animal vaccination may be found a method wherein lies the remedy for both; that is, the avoidance of syphilitic contamination and the capability of indefinite multiplication of vaccine material.

The possibility has been suggested of communication of bovine disease other than vaccinia, especially of tuberculosis of the cow. Tuberculosis is known to be inoculable, as demonstrated by Villemin, and more recently by the experiments of Koch and many other experimenters. Inoculated tuberculosis starts from the point of its insertion, as shown by experimentation upon the guinea-pig, rabbit, and other animals. It may be transmitted by means of the tubercle bacilli present in a tubercle itself, in the blood of an infected animal, or in the air exhaled from a diseased lung. Upon this point Dr. Warlomont says: "The importance of these facts as related to bovine, as well as to humanized vaccination, is worthy of consideration, and one fact should be stated at the outset, that it is impossible to inoculate tubercle by means of *superficial insertion* of bacilli which is the usual method of the insertion of vaccine lymph. The latter develop very slowly, and cannot, like those of splenic blood, rapidly infect a small wound. If we desire to make an animal tuberculous, we must carry the bacilli deeply into the tissues. Thus it is explained why it is that no one has been infected while making autopsies of

Fig. 4251. Charging Ivory Points. (By permission of the H. K. Mulford Company.)

tuberculous subjects. Thus, *a fortiori*, is it explained why no one has ever been infected with tuberculosis through vaccination. . . . So much for theory; now for the practice. Let them show, among the millions of subjects vaccinated in the past twenty-four years, either with humanized or with bovine lymph, a single case that has exhibited, at the spot of insertion of vaccine lymph, anything that resembled a tubercle. Nothing of the kind has ever happened, although it is probable that, among so large a number of inoculated persons, some must have received vaccine from tuberculous vaccinifers."

With reference to transmission of diseases of the "charbon" type, Dr. Warlomont states that "it has been completely demonstrated that laudable vaccine vesicles would never develop in animals affected with charbon. These affections are not common in animals sold at markets or elsewhere for purposes of vaccination."

All of these difficulties, if they are worthy the name of difficulties, may be avoided by the method adopted in the best establishments at present, which consists in delivering or using the lymph from any animal for the purpose of vaccination only after such animal has been proven by autopsy to have been absolutely healthy.

Government Production of Vaccine.—The production of vaccine lymph for the use of sanitary authorities in foreign countries is very generally conducted by the governments of these countries, or under their direct supervision.

In Sweden, a central establishment at Stockholm, under the direction of the Council of Health, furnishes vaccine for the whole kingdom. In Germany all the establishments are under the general supervision of the Imperial Board of Health.

In England an establishment is maintained at London under the direction of the medical officer of the Local Government Board. In Italy there is maintained at Rome a national establishment which distributes lymph to any province which desires it. But the provinces may establish their own plants, or obtain supplies from private parties under careful restrictions.

In France vaccine is supplied by private parties, but the work has the strong support of the Academy of Medicine.

In Austria the supply is partly from public and partly from private sources.

The cities of New York and Chicago maintain vaccine plants for the public use of these cities. There can be no reasonable objection to the establishment of such plants either by a country, State, or large city. In fact, the objections which are always liable to arise in consequence of the sharp competition of private producers are thus avoided. There is also the advantage that a State in which no private establishments exist may produce its own vaccine, under its own control, and in such place as may be readily accessible in times of emergency.

The Question of the Degeneration of Vaccine.—The question whether vaccinia, in its transmission from the cow through a series of human beings year after year, loses any of its primary efficiency has been a subject of discussion since the earlier years of the present century.

Jenner did not admit such a possibility, although frequent applications were made to him, within two or three years after his discovery, for lymph "as recent from the cow as possible." A further experience of twenty years satisfied him that the hypothesis of such degeneration was groundless. He was, however, careful to require that the successive transmissions of lymph should be made through healthy subjects. In 1816 he stated that "the matter may undergo a change that may render it unfit for further use by passing even from one individual to another, and this is as likely to happen in the first year of vaccination as in the twentieth." But that with proper care and attention lymph underwent no change he considered to be proven, by the fact that the vesicles he was then producing were "in every respect as perfect and correct in size, shape, color, state of the lymph, period of the appearance and disappearance of the areola, its tint, and, finally, the compact texture of the crust, as they were in the first year of vaccination; and to the best of my knowledge, the matter from which they were derived was that taken from a cow about sixteen years ago."

The argument as thus stated was, that if lymph could undergo eight hundred or nine hundred transmissions through men without giving evidence of change, it should also remain equally unchanged after an indefinite number of such transmissions, and many observers after forty years declared the same opinion.

The National Vaccine Board of England, in their annual report for 1854, declared "that the vaccine lymph does not lose any of its prophylactic power by a continued transit through successive subjects."

Seaton confirms the truth of this statement in his "Handbook," page 203.

In the United States one of the most noted instances of long-continued transmission of humanized lymph is that recorded by Dr. E. M. Snow, superintendent of health of Providence, R. I., and his successors. In a report published by Dr. C. V. Chapin in 1886 he said: "The record of the vaccine now used in the public vaccinations in this city may be traced from arm to arm by name and date continuously back to February 29th, 1868; a date fully two years before the importation of the famous Beaugency stock of animal virus, from which the country has since been so largely supplied." He states, furthermore, that "all the traditions concerning the matter are to the effect that the virus then in use was of the stock sent to this country to Dr. Waterhouse, of Cambridge, by Dr. Jenner in the spring of 1801, with the statement that it was from his original stock."

The theory that vaccine lymph has suffered degeneration by successive transmissions through the human species is chiefly of continental origin. Many French authorities have affirmed this principle as a reason for frequently resorting to the cow for a renewed supply of lymph. Kinglake also, in England, as early as 1814, had advanced the theory of degeneration.

The Royal Academy of Sciences of France in 1838 offered a prize of ten thousand francs for the best essay on this subject, thus indicating the importance which was attached to the problem at that early day. It was not till 1845 that a report was made on the thirty-five essays received. The prize was divided between Bousquet, Fiard, and Steinbrenner, each of whom answered the question affirmatively. The Sanitary Commission of the Grand Duchy of Baden in 1817 reported in favor of a frequent resort to the cow, in consequence of the degeneration of lymph.

The Technique of Bovine Vaccination.—The best animals for use in bovine vaccination are calves and heifers, from the age of one month to two years. Warlomont says "they should weigh at least 100 kgm. (220 lbs.), and be in good health."

The recent German regulations state that calves of "five weeks and upward are to be preferred." (Dr. Voigt, of Hamburg, employs calves from three to four months old.)

Vaillard prefers calves from two and a half to three months old, and gives as a reason the consequent avoiding of tuberculous stock. M. Leclerc, the chief inspector at Lyons, had met but five tuberculous calves out of about four hundred thousand slaughtered animals.

The stock selected for the purpose of vaccine propagation should be in perfect health, and if fatigued by long travel on the railroad, or affected with diarrhœa from improper feeding, they should be allowed to rest for a day or two until they are in good condition, before being submitted to vaccination.

The stable should be well ventilated and kept at a medium temperature. For young animals the feed should be mainly of milk, and for older animals hay and the lighter meals may be used. In Holland, the feed of calves at vaccinating establishments consists of ten litres of milk, and from two to four eggs daily, for each calf.

Older animals are often used for the propagation of

vaccination apparently having no effect upon the quantity or the quality of the milk. Such animals present the disadvantage of large size and consequent difficulty of management. If a large yield of lymph is desired for the use of [illegible] of lymph may be made without laying the animal upon itself in the fact that a small percentage of milk-giving cows, and especially of the older animals as found [illegible] value of the animal, either alive or as slaughtered for [illegible] should be received as authority. "We must, it is not forget that, at the latest, the animal should yi its harvest in the course of the sixth day, and that it be killed on the seventh, before the possible development of suppurative fever. As a matter of fact, it does not suffer in consequence of vaccination, however numerous the insertions may be. It may suffer from the fatigues and ill-treatment of the journey, from the maneuvers of the dealer, from change of stable, or from its separation from the mother, but vaccination of itself by no means the cause of any depreciation in the animal. This may be [illegible] sibility."

In Russia, [illegible] sold to the Jewish rabbi to be slaughtered as food. A larger price is paid for them than for ordinary calves, owing to the fact that they are in excellent condition as a result of good [illegible]

Animals vaccinated upon the abdomen may injure the vesicles by abrasion against the floor, an accident which may be prevented by the use of Tegmin bandages. These have been introduced [illegible] the Germans [illegible] to be universally satisfactory.

The [illegible] under conditions of scientific cleanliness, such as are prescribed by the Germans [illegible] Germany. The construction and administration of the stabling for the calves. 2. The means for washing or bathing calves before their vaccination. 3. The construction and cleansing of the [illegible] 4. The cleansing of the [illegible] with [illegible] 5. The [illegible] 6. The [illegible] 7. The [illegible] 8. The [illegible] 9. The [illegible] 10. The [illegible] 11. The [illegible] 12. The [illegible] 13. The [illegible] 14. The [illegible] 15. The [illegible] 16. The [illegible] 17. The [illegible] 18. The [illegible] 19. The [illegible] 20. The [illegible] 21. The [illegible] 22. The [illegible] 23. The [illegible] 24. The [illegible] 25. The [illegible] 26. The [illegible] 27. The [illegible] 28. The [illegible] 29. The [illegible] 30. The [illegible] 31. The [illegible] 32. The [illegible] 33. The [illegible] 34. The [illegible] 35. The [illegible] 36. 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Fig. [illegible] [illegible]

continental vaccinators have chosen the inguinal region as the point of election. Lanoix, Depaul, and Chaudo preferred this region, including a space from 6 to 8 in. [illegible]

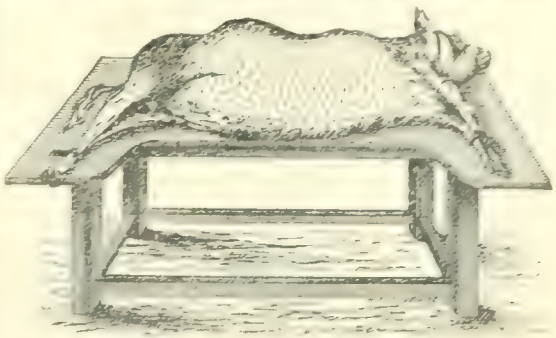

Fig. [illegible] [illegible]

posterior line running near the umbilicus below, and above by a horizontal line connecting the middle of the axillary fold with a corresponding point behind. Upon [illegible] this region lying in the risk of soiling.

For the fixation of the animal in a convenient position for the requisite operations, a tilting table will be found [illegible] for [illegible]

securing the animal to the table, for which purpose he employs five assistants, the duties of each being carefully defined.

Two of the forceps in common use are shown in the accompanying cuts. Fig. 4934 is that of Chambon, and Fig. 4935 that of Warlomont.

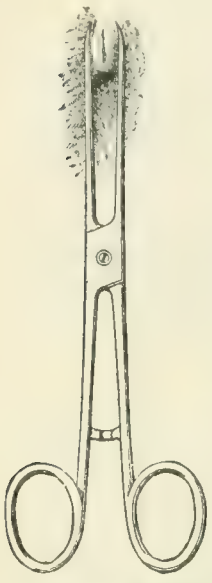

FIG. 4934.—Chambon's Expression Forceps.

A slight pressure only is necessary to hold the vesicle and facilitate the flow of lymph, and it often happens that no forceps are necessary.

The Development of the Vesicle.—If the inoculation is successful, each incision will begin to show a light red border at the end of about forty-eight hours; at the end of another day a slight swelling appears, increasing in size; and by the end of the fifth day a well-formed vesicle will be seen at the seat of each successful insertion. These vesicles are shaped according to the method of insertion. In the case of punctures they are circular, and in the case of incisions they are shaped like the half of an "elongated coffee-berry," having a cicatricial depression, surrounded by a zone of silvery white, and encircled by an outer zone of a reddish hue, the distinctness of color varying with the amount of pigmentation of the skin at the places of insertion. The swelling of the vesicle increases until about the seventh or eighth day, when the transparent zone becomes yellowish in color, and in the following days the vesicle becomes purulent, dries up, and is converted into a brown crust, which falls off from the fourteenth to the twentieth day.

According to Warlomont, if the modes of insertion by incision and by puncture be practised on the same animal, the eruption will be developed twenty-four hours later in the latter, a circumstance which may prove of advantage, by having two stages of development in the same animal, and by the consequent possibility of collecting mature lymph on two successive days if necessary.

The proper time for the collection of lymph is a period of about twenty-four hours in length, and in order to obtain lymph of the best and most efficient quality, the opportune moment for collection should be carefully studied. This moment is not of necessity the time when the most abundant flow takes place, but an earlier period. For greater clearness of expression, it is best to state the period in hours, since the expressions, third, fourth, fifth day, etc., are differently interpreted by different writers.

Negri often made use of the vesicles of three times twenty-four hours. Throughout the continent, it is common to make the collection of lymph either at the termination of three, four, five, or six times twenty-four hours. At Cologne it is the practice to vaccinate on Tuesdays and collect lymph on Fridays. The more common custom in the United States was, previous to 1890, to collect lymph at the end of seven times twenty-four hours, or on the same day of the week with its insertion; or, if the collection required several hours, to complete the operation at that time, after the method employed by Lanoix. In most United States establishments, however, lymph is now collected at an earlier date.

Collection of Vaccine Lymph.—The vesicles propagated upon bovine animals usually require more pressure, in order to obtain a supply of lymph, than is necessary in the collection of humanized virus, especially from the arms of infants, in whom the skin is tender. From these the lymph usually flows readily at the slightest puncture or incision. In bovine animals, however, having a skin of greater thickness, considerable pressure is usually required to cause a free flow of lymph (see further statement in description of the establishment at Cologne).

Delivery of the Lymph.—A careful record is kept at each establishment of the date of sending, quantity, recipient, and other important items. By far the greater quantities were furnished in the months of May and June. The recipients were classified into public vaccinators, private physicians, and military physicians. The former class used by far the greatest quantity of lymph.

Sending and Packing of the Lymph.—The usual mode of sending lymph from the stations in the German cities is by mail in capillary tubes, usually containing about enough for five vaccinations, and in large glass tubes containing fifty or one hundred such portions. These are securely packed in wooden or pasteboard boxes, with directions for use accompanying them.

In most of the cities, test vaccinations were made upon calves for the purpose of proving the efficiency of the lymph before forwarding it. In times of unusual demand, however, this practice was omitted.

The Efficiency of the Vaccinations.—The results are stated with great care, both as to the number of persons vaccinated, and as to the number of insertions or separate scarifications made.

In Leipsic observations were made upon 22,158 primary vaccinations, in which the successful vaccinations amounted to 21,982, or 99.21 per cent.; partially successful, 145, or 0.65 of one per cent.; and unsuccessful, 31, or 0.14 of one per cent. Of the revaccinations, 15,115 out of 16,706, or 90.48 per cent., were successful.

In Hamburg, in a series of ten years the success rate of primary vaccinations was fully 99 per cent.

In the entire German Empire the success rate of primary vaccinations in 1899 was 96.1, or 1,446,914 successful vaccinations out of a total of 1,505,698.

Duration of Efficiency.—Lymph, when carefully preserved at an even and low temperature, retained its efficiency for from two to four months, and even longer.

Lymph used at stations was usually quite fresh, but private physicians often found it efficient at the age of several months. Tests were made at Stettin of lymph, 46, 81, 102, 138, 153, 175, 178, 229, and 249 days old, and in each case it was found to be efficient. The lymph was preserved in glass tubes.

FIG. 4935.—Warlomont's Expression Forceps.

Some lymph was sent to Madras from Berlin, February 17th, 1891, and a calf vaccinated with this lymph on the 17th of March, had one hundred and one good vesicles out of one hundred and twenty-one insertions. This was also successfully transmitted from this calf to others. In some cases lymph sent to places in hot climates proved without effect.

Diseases Following Vaccination.—Vaccine physicians are instructed to make special observations upon this point. Out of the immense number of vaccinated persons in Germany, but very few cases of erysipelatous eruptions, swelling of the axillary glands, and slight skin eruptions of a temporary character were recorded, and no cases of syphilis were mentioned.

Preparation of Lymph.—The following account of the method of preparing vaccine lymph at Berlin is given by Prof. Albert Guttstadt, in an article entitled "Das Impfwesen in Preussen in 1887-88," in the *Zeitschrift des Königl. Preuss. Statistisch. Bureaus*, 1890."

The skin of the calf is first washed with warm soap and water. The incisions then show clearly, and the lymph is taken out with a sharp spoon, shaped like a potato borer.

The lymph was at first mixed with glycerin in a porce-

lain mortar, but afterward a machine was employed which was designed by the assistant, Dr. H. Döring.

This apparatus, the "Döring lymph mill" (Fig. 4936), is the result of several trials, and consists of an iron

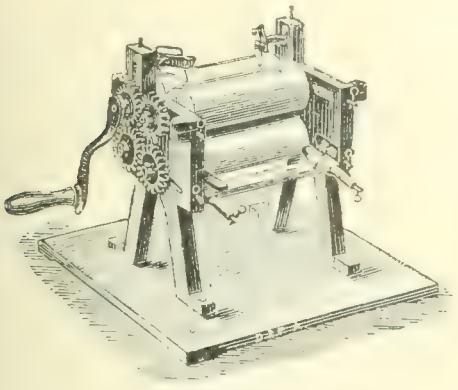

Fig. 4936.—Döring Lymph Mill.

frame fastened to an iron plate, supporting four cylinders of porcelain having roughened surfaces. These cylinders are removable, and may be sterilized.

The lymph is first mixed by light stirring with one-third of its weight of glycerin, and is then placed on the line of contact between the cylinders, a little at a time, while an assistant turns the handle. In a few moments the finely mixed lymph mass is scraped off from the last cylinder by the glass shield and caught in the dish below. After the whole mass has passed through the apparatus it is stirred with a glass rod, with the addition of more glycerin, and is passed through the mill again. It is advisable, after emptying the lymph upon the cylinders, to scrape the dish to avoid loss. The lymph is then ready for use. The loss is at the utmost 0.5 per gram. From 20 and 25 gm. of raw lymph may thus be easily prepared for use in thirty-five minutes.

The apparatus, exclusive of the plate on which it stands, is about 20 cm. (8 in.) in each dimension. Accompanying each apparatus are two rectangular dishes and glass scrapers, a spatula to collect lymph, a clamp, screwdriver, and oil can. The apparatus is sold by Julius Schober, Adalbert Street, 39, Berlin.

Another machine employed for the same purpose is that devised by Dr. Chalybäus, of Dresden. It consists of a vertical spindle revolving in a cylinder, the material for trituration being fed through a funnel at the top.

Vaccination in Japan.—Vaccination has made rapid progress in Japan since its introduction there. It appears from the government reports that calf lymph is now very largely used. The vaccine farm was at first under control of the Government, but was finally entrusted to a private association. February 16th, 1888, a commission was appointed to investigate the subject of the preservation of lymph, so that it could be distributed to distant places and still be used with efficiency.

1. *Vaccine Lymph in the Dry Condition.*—(*a*) On ivory points. The points in use in the United States at present are of a pretty uniform size, being about 37 mm. in length, 6 mm. in width, and about $\frac{1}{2}$ mm. in thickness. By far the greater number are produced at several establishments in Connecticut, where bone points of the same size and shape are also made for the same purpose, at less cost. Larger and smaller sizes have also had a limited use. One end of the point is usually made square and the other end pointed, and the rounded edges near the point are often bevelled, this device having been adopted for the purpose of allowing the point to be used as a lancet (Fig. 4923).

In order to charge the points, they should be applied to the lymph exuding from the vesicle, first upon one side of the point and then upon the other, until they are quite uniformly coated with the lymph for a distance of from 1 to 2 cm. from the point. In the case of some propagators, it is customary to allow the points to dry, and to recharge them with lymph, either from the same or from another animal. The points should be carefully laid to dry upon the edge of any convenient place, where the charged portion may project in such a manner as to allow of its drying readily. Ivory vaccine points are adapted to use in connection with the method by scarification, rather than by puncture. As ordinarily prepared, the lymph upon ivory points will usually retain its activity, when the points are kept at an even, cool temperature of 40° to 60° F. (4° to 15° C.), for two months or more. They have been known, however, frequently to retain their activity for very much longer periods, ten months or more having been reported. Points are also charged with glycerinated lymph, and are then coated with paraffin, or protected by a shield of glass or other material.

An ingenious device was brought to notice by Dr. F. Kimball, of Andover, Mass., in 1880, for the purpose of facilitating the rapid application of lymph to ivory points when considerable quantities are required at once (see Fig. 4937). It consists of two pieces of pine wood glued together in such a manner as to allow the points to be held firmly in position while the lymph is applied. A thin shaving of uniform width is removed from one of the pieces of wood, not quite as thick as the points. Similar devices are now in use in some of the larger American establishments.

Various methods are employed for packing charged points for transportation. Those methods are best which most efficiently protect the points from the air, from moisture, and from changes of temperature. In the method employed by Dr. Martin the points are first wrapped with clean absorbent cotton, then with thin white paper, and finally are wrapped in an outer coating of thin sheet gutta-percha, which is easily made perfectly tight by a very moderate degree of heat.

(*b*) *Crusts.*—This method of using vaccine material has, fortunately, gone out of use in places where bovine lymph can be obtained, and it should be abandoned altogether, as relating both to bovine and to humanized lymph, since the crust consists of the products of the vaccine vesicle which have passed the period of maturity, when the clear transparent lymph has advanced to the purulent stage and the vesicle has become a pustule.

A few years since, bovine crusts were offered for sale in the shape of masses, or cones, which consisted of powdered crusts, formed into shape by the aid of pressure and other means; examination showed that these masses contained a considerable quantity of foreign material, such as might be expected to be found in the crusts formed upon animals which had not been carefully kept.

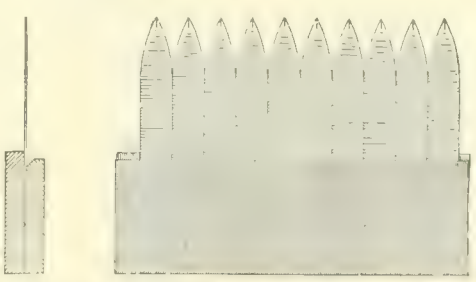

Fig. 4937. Kimball's Device for the Rapid Collection of Lymph.

Serious results following the use of these devices soon put an end to their use.[13]

It is hardly necessary to allude to the fact that crusts, like other organic material, undergo rapid putrefactive changes in the presence of heat and moisture. Instances are on record of serious injury from so-called vaccinations made by the use of crusts kept dissolved in water for a considerable period.

Other methods employed in the early part of the nineteenth century were the use of bits of thread or silk saturated with vaccine lymph, and these were drawn under the skin and allowed to remain till infection took place.

Bits of goose quill were also sharpened like a pen and then charged with lymph. These were often used for vaccinating by puncture.

(c) *Dried Vaccine Lymph in the Form of Powder.*—This method of using vaccine lymph has been employed to some extent, but has not come into general use. M. Ciaudo says he has obtained good results with dried vesicles after from one hundred and ten to one hundred and thirty days. Warlomont experimented with vesicles cut into small fragments and rapidly dried in a drying apparatus. These fragments at the end of two or three days were reduced to a fine powder and preserved in tubes closed only with cotton. When the powder was used in this condition the vaccinations were not very successful; but if the powder was allowed to macerate in glycerin and water for twenty-four hours (thus allowing the vaccine microbes to pass from a latent state to one of active life) and was then used, good results were obtained, even though the powder was more than three months old.

2. *Vaccine Lymph in the Moist Condition—Pulp.*—This method, first introduced by Ciaudo, of Milan, consists in excising the vesicles, freeing them from all detritus, making a homogeneous paste, and adding to each vesicle 0.5 gm. of chemically pure glycerin; this is placed in a small glass vial, and covered with more glycerin to exclude the air.

Vaccine material thus prepared preserves its activity for a long period, and is very efficient. Its effects are, however, occasionally quite irritant. A similar mode is adopted in Holland, the pulp being preserved between glass plates.

In Germany it is customary to employ capillary tubes for single vaccinations, but when large quantities are required, the glycerinated emulsion is put into small vials holding enough for twenty-five to fifty or one hundred vaccinations in each. Glass plates, slightly excavated and fitted with tight covers, are also in use.

Capillary Tubes.—These were first brought to public notice by Dr. Husband, of Edinburgh. Their essential characteristics were stated to be as follows: (1) They should be so slender as to admit of ready sealing in the flame of a lamp; (2) they should be large enough to contain lymph sufficient at least for one vaccination; (3) they should be long enough to admit of sealing without subjecting their contents to the heat of the flame; (4) they should be strong enough to admit of handling without breakage. Dr. Husband advised the following dimensions: Average length, 2¾–3 in. (about 7–8 cm.); diameter, $\frac{1}{25}$ in. (about 1 mm.). Another form is made with an enlargement at the centre of the tube. Tubes are sometimes made with closed ends, that the interior may be kept clean until ready for use. When required for use the ends should be broken off, a small rubber bulb applied, and the lymph should be blown out upon a glass plate, from which it may be conveyed with the lancet to the scarifications. Tubes should be used only for the preservation or storage of glycerinated lymph.

Glycerinated Lymph.—As early as 1850 Mr. R. Cheyne[14] had called attention to the superiority of vaccine lymph which has been treated with glycerin. Curschman, however, credits Müller of Berlin with this discovery. Warlomont of Brussels refers to the subject in his "Traité de la Vaccine" and had patented a process of such mixture in 1882.

The German Government also recognizes this process in the regulations issued April 28th, 1887.

Chambon, Menard and Straus,[15] of Paris, also by means of experiment, arrived at similar conclusions. So also did Leoni, Klein, Kitasato, and others.

Dr. Copeman[12] sums up the advantages of glycerinated lymph as follows:

1. By employing the method of glycerination of lymph pulp great increase in quantity can be obtained without any consequent deterioration in quality, the percentage of insertion success following in its use being equal to that obtained with perfectly active fresh lymph.

2. Glycerinated lymph does not dry up rapidly, as does unglycerinated lymph, thus simplifying the process of vaccination.

3. Glycerinated lymph does not coagulate, so that it never becomes necessary to discard a tube on this account.

4. Glycerinated lymph can be produced absolutely free from the various streptococci and staphylococci which are usually to be found in untreated calf lymph, and which are, under certain circumstances, liable to occasion suppuration.

5. In like manner the streptococcus of erysipelas, in the event of its having been orignally present in the lymph material, is rapidly killed out by the germicidal action of the glycerin.

6. The tubercle bacillus is effectually destroyed even when large quantities of virulent cultures have been purposely added to the lymph.

7. The possibility of inoculation of syphilis is eliminated, as the calf is not subject to this disease.

8. The necessity for collecting children together, with the attendant risk of spread of infectious diseases, or of transporting a calf from place to place, is obviated, while the danger of "late" erysipelas in the child is diminished by reason of there being no necessity to open the mature vesicles for the purpose of obtaining lymph.

9. The bacteriological purity and clinical activity of large quantities of lymph can be readily tested prior to distribution.

10. By reason of the possibility of keeping large stocks of glycerinated lymph on hand for considerable periods of time without appreciable deterioration, any sudden demand, such as is likely to arise on the outbreak of epidemic smallpox, can be promptly met.

11. The expense of producing glycerinated lymph is proportionally small, since the amount obtainable from each calf is enormously increased.

With reference to the question of quantity Dr. Copeman further observes: "It is no unusual thing abroad to provide from a single calf an amount of glycerinated lymph that shall serve for four thousand and six thousand vaccinations, and in Berlin we were assured that the glycerinated lymph which was prepared in our presence from one calf, would suffice for no less than fifteen thousand vaccinations" (p. 192).[12]

Upon the subject of the duration of activity of glycerinated lymph Dr. Copeman also states: "Glycerinated calf lymph can be prepared which becomes freed from extraneous organisms, is available for a large number of vaccinations, at least five thousand from an average calf, and retains full activity for eight months, and will, under favorable circumstances, continue to do so in all probability for still longer periods if necessary" (p. 186).

Description of the Vaccine Establishment at Cologne.—This new vaccine plant, erected about 1895, was built as a matter of convenience near the new cattle and slaughtering establishment of Cologne.

In building the new establishment the provision of a suitable annex for the production of lymph was borne in mind from the very first; and so the present institution originated, which meets all the demands of hygiene, and may justly be regarded as the prototype of such institutions.

The building is very solidly built, but undercellared only, and to the smallest extent on the eastern side. As, however, the whole of the ground was filled in, and only absolutely dry and permeable material employed, there is no fear of any dampness of the rooms.

On the ground floor of the building are the corridor, collecting-room, calf stable, slaughter-room, doctor's room, office, and a closet.

On the upper floor, which is reached from the collecting-room by a convenient winding staircase, is the laboratory, adjoining which, on both sides, is a large garret. The calves are driven into the station through the doorway

of the slaughtering-room, which lies at the opposite end of the building. (See Fig. 4938.)

While the floors of the slaughtering-room, calf stable, collecting room, and laboratory are of concrete, the doctor's room and the office have inlaid wooden floors (parquetry); the corridor and closets are laid with "Mettlacher" tiles; and, finally, the rooms in the roof (garrets at the sides of the laboratory) are laid with floor boards. In the calf stable, slaughtering-room, and collecting-room the floor is slightly sloped in one direction, and at the lowest point there is a drainage outlet which is shut off by a small intercepting trap. The collecting-room, calf stable, and closet are lined, to the height of 1.5 metres from the floor, on all four sides, with white opaque glass tiles; the slaughtering-room on three sides (the door side is excluded) to the same height with white glazed tiles. The remaining part of the walls of these rooms is painted with white porcelain enamel. The walls in the doctor's room and the office are papered. In the laboratory and corridor the walls are painted with oil paint. The collecting-room is brightly lighted by a window 4 metres wide by 3 metres high. The light entering becomes strongly reflected by the brilliant white walls. The laboratory has three windows, the calf stable two, and the doctor's room and office one large window each. The closet and slaughtering-room have each one small window. All the rooms are, therefore, amply lighted.

The calf stable contains eleven stalls for the reception of calves. Upon the space which would correspond to the twelfth stall a weighbridge is sunk, enclosed with the above-described iron work; this machine allows of the calf being weighed while being taken through. The hollow in which the weighbridge stands has also a smell preventing arrangement. The ventilation of the stable is obtained by a large tube which passes through the garret above. The doors, padding, and air draught isolate the collecting-room both from smell and from noise. Between the calf stable and the collecting-room there is an arrangement of double doors, one of which is thickly padded. Water is supplied by the city main, and in every room a sink is provided. The lighting is by electricity; in the laboratory, however, the "Auèrches Glühlicht" (a form of incandescent light) has been found preferable.

The heating is effected by means of American stoves. Large gas stoves serve for the heating of the water and milk. For the storage of considerable quantities of lymph a sufficiently large room is reserved in the refrigerating house of the city cattle establishment.

The laboratory is completely fitted for bacteriological investigations, containing all sterilization apparatus—thermostats, an excellent microtome, microscopes, centrifuge, etc.

The extent of the lymph production may be understood from the following figures: In the year 1894 about 356,000 portions of lymph were issued, and in this year (1895) about 400,000.

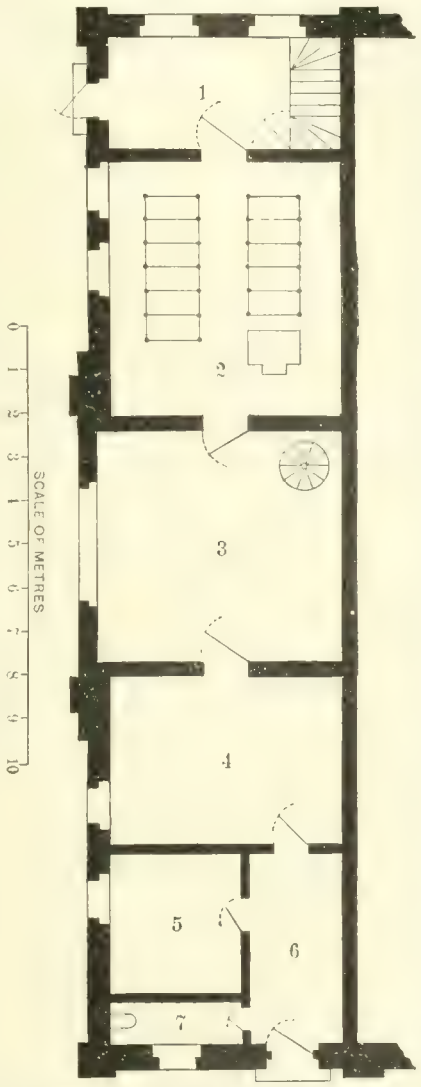

FIG. 4938. Plan of Cologne Vaccine Station. 1, Slaughtering-room; 2, calf stable; 3, vaccinating-room; 4, medical director's room; 5, clerk's room; 6, entrance hall; 7, closet. (From *Centralblatt für allgemeine Gesundheitspflege.*)

Calves.—The calves range usually from about six to eight weeks old. They are purchased in the meat market which immediately adjoins the establishment. The calves required for the current week are bought on Monday, and they are sold on the following Saturday, after their slaughter and the collection of lymph on the previous day; so that the stable is always empty from Saturday to the following Monday. The calves are kept under observation in the stable for twenty-four hours after their reception, and are vaccinated on Tuesday. *Only three complete days* are allowed for the progress of the local results of vaccination. On Friday the animal is slaughtered in a small slaughter-house opening off from the stable, and immediately it is dead the carcass is brought into the collection-room on a trolley, the abdomen washed, and the epithelial pulp of the vaccination area is removed by means of a sharp spoon.

Vaccination of Calves.—The process of vaccinating the calves is carried out in a fashion similar to that employed at the Berlin and Dresden stations, namely, by long parallel incisions over which glycerinated lymph is rubbed by means of a spatula or other flat-bladed instrument. The lymph employed for vaccination of calves is always kept for a period of at last six weeks after glycerination, in order to insure that it shall be as free as possible from extraneous organisms before it is used to vaccinate the calves.

After collection of the lymph pulp, and while it is being prepared for use, the carcass of the calf is taken back to the slaughter-room, where it is skinned and opened. The internal organs are removed and brought in on trays to be examined by the veterinary surgeon. In the event of his forming an opinion that any of the organs presented any condition indicative of disease, the lymph derived from the animal in question would be at once destroyed.

In view of this precautionary measure it is not deemed necessary to test the calves by the injection of tuberculin prior to their vaccination.

Collection and Preparation of Lymph.—The greatest amount of vaccine is collected during the months of March, April, and May, when from six to eight calves are employed every week. For the remainder of the year the weekly vaccination of one or two calves is found to be sufficient to supply all the lymph required for human vaccination and revaccinations in the Cologne district.

In the preparation of lymph material the epithelial pulp from the vaccinated area is removed by scraping with a Volkmann's spoon, and is received in a small glass dish. In this it is weighed, after which it is turned out into a mortar and thoroughly triturated; at first, without any addition of water or glycerin; later, small quantities of water are gradually added to the extent of five times the weight of pulp. The mixture having been

ground up still further, double the quantity of glycerin is finally incorporated. Thus, at the time of our visit, 10 gm. of pulp having been collected from one calf, the composition of the finished emulsion was as follows: Pulp, 10 gm.; water, 33.5 gm.; glycerin, 66.5 gm. Dr. Vansclow informed us that this quantity would suffice for the vaccination of five thousand children.

FIG. 4939. Volkmann's Spoon.

The emulsion is afterward forced into small bottles and tubes by means of a machine actuated by water power. This machine, which is manufactured by a Vienna firm, appears to be decidedly useful and convenient and is capable of being worked in connection with any form of pressure apparatus.

The small bottles are of different sizes, and contain lymph sufficient for fifty, for one hundred, and for one hundred and fifty vaccinations respectively. The bottles and their corks are all of them sterilized prior to use.

We were struck with the numerous precautions which are taken in this institution to insure thorough asepsis throughout the various stages of lymph production. Thus, in the collecting-room the flooring is of cement concrete, the walls are lined internally for about half their height with opaque glass tiles, the upper half being of Parian cement.

On the first floor of the building is a bacteriological laboratory, which is reached from the collecting-room by an iron spiral staircase. It is fitted up with an autoclave, incubators, etc. But owing to the director being engaged in private practice, he has no time to work in this laboratory, which is, therefore, used only when it is desired to sterilize cloths, instruments, or glassware. With the lymph and pulp material collected and glycerinated in our presence on January 16th, 1897, Dr. Cory vaccinated 34 children on January 19th, with an insertion success of 98.8 per cent., and 21 children on February 11th, with an insertion success of 93.3 per cent. (Copeman's Lectures, pp. 225–228).

Plan of Model Vaccine Establishment.—The following plan of a model vaccine establishment is shown in Delobel and Cozette's "Vaccine et Vaccination," Paris, 1899. The general plan is that of an open court surrounded by apartments, stables, etc., suitable for the purposes of producing vaccine material from animals.

This establishment is about 77 feet wide by 155 in length, and may be made much smaller by the omission of the two large director's rooms (intended in the original plan as a living-room) and the horse stable and carriage-house, as circumstances may require. Rooms 8 and 9 are found to be convenient in those cities where vaccination with fresh lymph is practised at the establishment as one of the functions of such a plant, a practice which was carried out for many years at the government station managed by Dr. Cory in London. (Fig. 4940.)

THE BACTERIOLOGY OF VACCINIA.—As early as 1809 Sacco[16] noticed the presence of granules in vaccine lymph. For a half century no further progress appears to have been made. As late as 1863 Eiselt of Prague described vaccine lymph as a contagious fluid devoid of cells. In 1866 Beale[17] drew attention to particles of germinal or living matter invading the tissues from the blood, which he identified as the virus contagium, or *materies morbi* of contagious diseases, and applied this principle especially to vaccine lymph. Hallier and Zurn,[18] of Jena, claim priority, and described in 1867 an abundance of micrococci as occurring in vaccine lymph. They also indicated the necessity for cultivation experiments to determine whether or no these micrococci stand in a causal relation to vaccinia.

Keber,[19] of Danzig, in 1868 also described micrococci in vaccine lymph. Cohn[20] in 1872 confirmed Keber's observations and distinguished the micrococci from the spores of moulds, and also differentiated them from bacilli. Cohn was not able to establish a difference between vaccine and variolous lymph.

It then became necessary to determine whether this particulate matter was essential to its specific action. Chauveau[21] attacked this question, and showed that the leucocytes in lymph are not essential to its specific action, since, after dilution, the supernatant fluid, free from leucocytes, was found to produce normal vesicles of vaccinia. On the other hand, by a carefully conducted experiment, he proved that if distilled water be cautiously

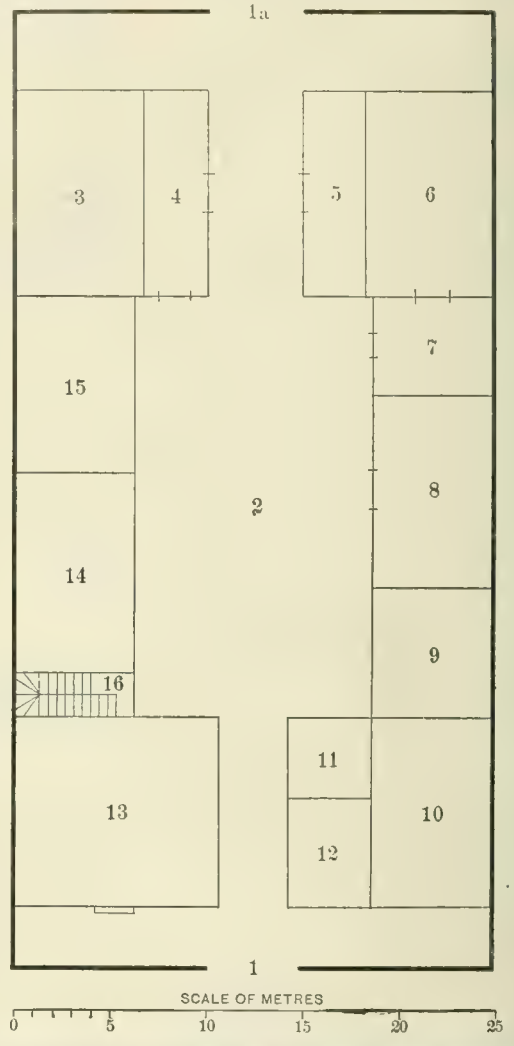

FIG. 4940.—Plan of Proposed Plant for Animal Vaccine Production. 1, 1*a*, Gates, one at each end. 1, Public entrance; 1*a*, entrance for animals; 2, open court; 3, stable for ten animals; 4, room for preparing the calves, shaving, etc., sufficient for one or two animals; 5, vaccinating-room, provided with one or two vaccinating-tables; 6, room for the vaccinated animals; 7, room for collecting the lymph; 8, vaccinating-room, for those who come to the establishment to be vaccinated; 9, waiting room; 10, laboratory; 11, packing-room; 12, clerical room, records and correspondence; 13, director's room; 14, carriage house; 15, horse stable; 16, stairway leading to the granary and room of employees.

floated on the surface of lymph in a small cylindrical vessel the soluble elements of the plasma will diffuse in the water, but the granular corpuscles remain in the lymph. The upper layers of the liquid, which have imbibed by diffusion the soluble albuminous matter of the lymph, are nevertheless totally inactive and incapable of

producing vaccinia. He therefore concluded that the active principle of the lymph resides, neither in the leucocytes nor in the soluble albuminous material, but in the suspended granular corpuscles of the lymph, that is, that the contagium is particulate. He showed further that lymph can be greatly diluted, and yet retain the contagium unimpaired, provided the greater the dilution the more extensive the absorbing surface. With a lymph diluted with about fifty volumes of neutral fluid a large proportion of vaccinations may fail totally; but in those which "take" the vesicles will not show any sign of attenuation or diminished virulence of the infective matter, but will be as large and as characteristic as those produced by undiluted lymph.

Sanderson[22] in 1870, in his report to the Privy Council, confirmed the experiment of Chauveau.

Copeman[16] has recently performed the experiment of filtering lymph through a Kitasato porcelain filter under pressure. The filtrate was absolutely sterile.

The hypothesis, therefore, that the active principle of vaccine lymph resides in its particulate elements rests on a very high degree of probability.

The flora of the lymph of vaccinia and variola have been thoroughly studied by Crookshank, Copeman, Blaxall, Buist, Fremlin, and others in England, by Cohn, Kleos, Koch, Pfeiffer in Germany, and by many others, and many micro-organisms have been isolated, several of which have been claimed to be specifically pathogenic, but no organism appears to have been discovered which has been proven to be the specific contagium of vaccine lymph. Of the various micro-organisms that have been discovered in lymph by different observers, the three most common are *Staphylococcus albus*, *S. pyogenes aureus*, and *S. cereus flavus*, which probably correspond to Buist's white, orange, and yellow vaccine. According to Copeman, one or another of these is to be found almost universally in every specimen of lymph examined.

Parallel with and in harmony with these investigations are the various experiments which have led to the adoption of glycerin for the purpose of preserving and diluting vaccine lymph, and of rendering it sterile, so far as concerns the presence of aërobic extraneous bacteria.

Cheyne[14] in 1850 and 1853 first demonstrated the fact that the activity of vaccine-lymph could be preserved for at least six months by the use of glycerin, and that its activity appeared to be increased rather than diminished by this means.

Müller,[23] director of the Berlin vaccine institution in 1866, confirmed Cheyne's experiments, and showed that such dilutions could be transmitted to distant countries and tropical climates without impairing their activity.

Copeman[24] again confirmed these experiments in 1891. In 1892 Chambon and Menard[15] found that while fresh glycerinated vaccine pulp gave only moderate results, the same emulsion kept for a fortnight caused a fair eruption, and at the end of forty, fifty, or sixty days produced a crop of typical vesicles.

Copeman found that a sample of glycerinated calf lymph forty-two weeks old gave in Dr. Cory's hands an insertion success, based on fifty insertions, of one hundred per cent.

Farrar[16] therefore concludes that prolonged glycerination secures the gradual extinction of all extraneous saprophytic microbes, that whatever be the nature of the contagium of vaccinia it is not an organism which can be cultivated by aërobic methods in ordinary laboratory media, and that no microbe isolated down to the year 1892 had any claim to be considered specific.

Crookshank[24] indorses this opinion, and says that no evidence is to be obtained by present methods as to the bacterial nature of calf lymph. He therefore suggests that a different line of inquiry may throw more light on the subject.

Other Theories.—Protozoa.—Renaut[25] in 1881 noticed certain highly refractile bodies in vesicles produced by inoculating the corneæ of rabbits and guinea-pigs with vaccine lymph.

Guarnieri[26] in 1892 described these bodies and called them *Cytoryctes vacciniæ vel variolæ*, classified them as Rhizopoda, and claimed for them a specific action in vaccinia and variola. They are capable of reproduction. Monti,[26] of Pavia, identified the same bodies, and drew the same conclusions. Ruffer and Plimmer[27] independently examined the same bodies and established a close correspondence between them. The Pfeiffers,[28] of Jena, and Weimar,[29] Clarke,[30] and others also described these so-called parasites more carefully, confirming Guarnieri's hypothesis. It cannot be denied that by their delicate and careful work, they have made out a strong *prima-facie* case for the protozoon theory, which also derives much support from the analogy of malaria. But the malarial parasite is much more definite in shape and size, its developmental changes follow a regular and well-defined cycle, and the evidence of its being the specific etiological agent of malaria has been well established.

Ferroni and Massari[31] maintained, *per contra*, that bodies indistinguishable from the so-called parasites of Guarnieri could be identified in the epithelial cells after mere mechanical or chemical irritation, and that those bodies are either altered leucocytes or derivatives of the nuclei of the epithelial cells.

Salmon[32] examined these alleged protozoa and pronounced them to be merely chromatic masses derived from the migratory cells.

Attempts to cultivate protozoa have not met with success. Shattock and Ballance[33] in 1895 made many careful attempts at cultivation, but the results of all their experiments were negative. In 1892 a fresh impetus was given to the bacterial hypothesis by Klein,[34] who suggested that a bacterial organism might exist in vaccine and in variolous lymph latent in spore form.

Certain considerations favor this hypothesis: First. The action of glycerin appears to be germicidal only for cocci and sporeless bacilli, and is not inimical to the preservation of the spores.

Second. Lymph when dried after its collection from the vesicle preserves its efficacy for a long time, as well as or better than pure lymph stored in the fluid state. This fact suggests that active vaccine matter exists in the form of spores, since non-spore-bearing bacteria rarely retain their vitality when preserved for a long time in a thoroughly dry state.

Third. Lymph taken from the calf on the fifth, sixth, or seventh day, or from the human arm on the seventh, eighth, or ninth day, that is, when the vesicles are mature, retains its efficacy better than lymph taken at an earlier date, although such earlier lymph used directly from calf to calf or calf to arm is fully efficacious.

These facts are consistent with the existence of spores in the lymph taken at that particular date, and a microbe yielding spores as the last phase of its life history would be present in the earlier stages of vaccinia chiefly as a non-spore-bearing form, and in such form would withstand drying less well.

The earlier, therefore, we obtain lymph from the nascent vesicle the more likely we are to obtain the hypothetical microbe free from spores. By a special technique Klein succeeded in isolating a small bacillus, staining with difficulty, which there is fair ground for presuming to be the pathogenic organism of vaccinia.

Klein's method consists in prolonged staining with alcoholic gentian violet, by which he isolates a bacillus which he describes as occurring in cylindrical rods, fairly uniform in length, single, and occasionally in dumb-bells, 0.4 μ–0.8 μ in length, and one-third of this measurement in thickness. They are generally thicker at the ends than in the middle, and often include a spherical and slightly oval clear globule. They are to be found sparingly in lymph of the fifth or sixth day, more abundantly in that of the fourth day, and almost as a pure culture in lymph of the third day. Preparations of lymph taken from the calf seventy-two hours after vaccination contain bacilli chiefly in groups which look as though they came from an artificial culture. The later the lymph is taken the less numerous are the bacilli found. Klein made many attempts to cultivate this

bacillus in artificial media, but all attempts failed. This proves that the bacilli though constant in the lymph do not belong to the saprophytes that are occasionally present in lymph and are easily cultivable. Until this microbe can with certainty be cultivated, it cannot be submitted to the test of Koch's postulates, and its pathogenicity cannot, of course, be conclusively proven. Meanwhile, it would appear that there is a high degree of probability that it will turn out to be the specific agent in variola and vaccinia. This bacillus was also found in clear lymph from the vesicles of confluent smallpox of the fourth day.

Copeman claims to have cultivated the same or a similar bacillus by incubating for a long period—about a month—in eggs, and by inoculation of this upon calves he obtained a strain of lymph which was successfully used in the vaccination of calves and afterward of children.

After Chauveau had demonstrated that subcutaneous injection of vaccine lymph into the tissues is protective against subsequent vaccination (vaccinia sine exanthemate) Beclere, Chambon, and Menard[35] in 1896 proved that the serum of calves rendered immune by vaccination, and withdrawn several days or weeks after desiccation of the pustules, and inoculated into other calves in sufficient quantities (say 1,500 c.c.), renders these calves, if not absolutely, at any rate relatively, immune in a high degree to vaccination with lymph of proved potency.

Finally, Dr. Farrar concludes that the pathogenic identity of vaccinia and variola has been proved by the experiments of several workers. Klein's work on this subject is convincing. He showed that lymph originally derived from the vesicles of human variola and transmitted through calves would produce typical vaccine vesicles in calves and typical vaccinia in the human subject, the result being constant through several removes, and the calves so treated being insusceptible to vaccination with current calf lymph.

In the discussion which followed the reading of Dr. Farrar's paper Tavel,[16] of Berne, expressed the opinion that of all organisms hitherto found Guarnieri's *cytoryctes* would most probably be shown to be the specific etiological agent in vaccinia. He believed that the alleged discovery of a *sporidium vaccinale* by Funck, and the finding of certain protozoa by other experimenters were due to erroneous methods.

A new stimulus was given to the study of this most interesting question by the offer of a prize of £1,000 by the Worshipful Company of Grocers of London, in 1883. The problem being stated as follows: "To discover a method by which the vaccine contagion may be cultivated apart from the animal body in some medium or media not otherwise zymotic; the method to be such that the contagion may, by means of it, be multiplied to an indefinite extent in successive generations, and that the product, after any number of such generations, shall (so far as can within the time be tested) prove itself of identical potency with standard vaccine lymph."

The great importance of such an inquiry can scarcely be overestimated, since certain great advantages would thus be secured. On the one hand, the ability to produce unlimited quantities of vaccine material for immediate use in the face of an epidemic of smallpox, and, on the other hand, the ability to overcome the objections urged against animal virus of either sort, humanized or non-humanized, namely, the possibility of transmission of disease, however slight the foundation of such objections might be.

Experiments were conducted in this direction by Quist of Finland, by Dougall, and by S. C. Martin of Boston, but no practical conclusions appear to have been reached.

In harmony with this line of investigation are the investigations of Drs. Councilman, Magrath, Brinckerhoff, and Tyzzer. At a meeting of the Boston Society of Medical Sciences, April 28th, 1903, Dr. Councilman announced the discovery of the etiology of smallpox, and at the same time gave his opinion as to the identity of the disease with vaccinia.

He stated that smallpox passes though certain perfectly definite stages in its development on the clinical side, to which correspond equally definite changes in the form of the causative organism; that these changes in form consist first in the appearance in the cell protoplasm of small, homogeneously staining, structureless bodies, about 1 μ in diameter, not staining so deeply as nuclei, which gradually increase in size, coincidently with the degeneration of the cells in which they lie; that with this increase in size the character of these bodies changes, small granules surrounded by circles appear in them, the general outline becomes irregular, with increasing resemblance to an amœba; that a process resembling sporulation takes place with the breaking up of the amœboid forms into smaller, sporelike bodies; and that this constitutes the first cycle in the life of the organism. Up to this period the nuclei of the epithelial cells show no changes whatever, but the following alterations in these structures now appear: penetration of nuclei by the small sporelike bodies before spoken of, with the disappearance of such bodies from the cell protoplasm; small ring-shaped bodies become apparent in the nuclei; they also increase in size; the ring shape is at first preserved, which is soon surrounded by a spongelike body. This whole structure grows, fills, and finally destroys the nuclei, and the bodies become free; the bodies again become more homogeneous; ring-shaped bodies again become evident; finally each ring appears to have a central dot. These final bodies are regarded as the infecting agent of the disease. Two cycles of the organism, corresponding in general to what we know of the protozoa, have therefore been demonstrated: the first—extranuclear—simple, and the second—intranuclear—very probably sexual.

It also appears to be demonstrated by this work that vaccinia represents the extranuclear phase of the organism, but that the production of true smallpox is dependent upon the invasion of the nuclei—the intranuclear cycle. Vaccinia may be produced by inoculation, for example, in the calf or the rabbit; variola under similar conditions is produced in the monkey. This, also, Dr. Councilman and his colleagues have shown. The organism was found in the blood in one case. The difficulties of study are very greatly increased by the extreme rapidity with which the entire process takes place and by the ease with which the organisms are destroyed; the life history is completed with the formation of the vesicle, hence the absolute necessity of securing early and perfectly fresh material. The rôle of bacteria is regarded as entirely subordinate to that of the organism described, though the influence, particularly of streptococci, must be taken into consideration in the development of the disease.

Dr. Councilman expressed the opinion with confidence that the organism which he described as belonging to the protozoa was the essential etiological factor in the production of smallpox.

Proposed Investigations Relative to Vaccination.—The offer of a prize by the Grocers' Guild of London amounting to £1,000 has already been referred to, the object of this prize being to stimulate investigation in the direction of some possible medium of vaccine culture outside the living organism, either of man or of the lower animals.

A new line of investigation is also suggested by the Report of the German Board of Health of 1900, in which it is stated by the vaccine authorities of Hamburg, that they have reason to believe from the experience which they have had in the culture of vaccine lymph that it is possible to secure a much longer period of immunity from smallpox than has hitherto been possible by the employment of any vaccine lymph in ordinary use. They had arrived at this conclusion in consequence of certain observations relative to the percentage of failures in the revaccination of school-children in that city. It was observed that, for some reason, in 1894 the percentage of successful vaccinations among the revaccinated children in Hamburg suddenly fell off from an average of about 85 per cent. in the nine years 1885-93 to an average of only 67 per cent. in the six following years,

1894–99. That this decline in the percentage of successful revaccinations was not due to any deterioration of the lymph in use appears to have been proven by the fact that the high percentage of success among primary vaccinations conducted with the same lymph an average of fully 98.5 to 99.5 per cent.) continued throughout the entire period. The only explanation offered for this fact was that in consequence of employing a lymph of unusual strength in the earlier primary vaccinations, these children were rendered immune for a longer period than they would have been had ordinary lymph been employed, so that when they arrived at the legal age for revaccination the percentage of successful results was greatly diminished.[5]

This fact opens up a very interesting field of investigation with the view of strengthening the quality of vaccine lymph to such a degree as to prolong its immunizing power.

The following figures illustrate this singular fact in the experience of the Hamburg vaccine district:

RESULTS OF VACCINATION AND REVACCINATION IN HAMBURG DURING THE YEARS 1885–1901.—PERCENTAGE OF SUCCESSFUL RESULTS.

Years.	Primary vaccinations.	Revaccinations.	Years.	Primary vaccinations.	Revaccinations.
1885	99.8	85.8	1894	98.8	69.3
1886	95.4	78.9	1895	99.7	66.5
1887	98.9	80.2	1896	99.3	59.7
1888	99.8	83.4	1897	99.4	66.8
1889	99.8	87.7	1898	99.5	69.6
1890	99.7	90.1	1899	97.7	69.5
1891	99.4	89.3	1900	99.4	74.8
1892	99.0	87.3	1901	99.7	93.6
1893	99.6	82.9			

LAWS OF DIFFERENT COUNTRIES RELATIVE TO VACCINATION.—Herewith are presented the essential features of the vaccination laws of different countries in which vaccination has been introduced.

England.—The following are the essential provisions of the vaccination act of England as amended by further acts of 1871, 1874, and 1898:

(I) 1. The period within which the parent or other person having the custody of a child shall cause the child to be vaccinated shall be six months from the birth of the child, instead of the period of three months mentioned in § 16 of the vaccination act of 1867, and so much of that section as requires the child to be taken to a public vaccinator to be vaccinated shall be repealed.

2. The public vaccinator of the district shall, if the parent or other person having the custody of the child so requires, visit the home of the child for the purpose of vaccinating the child.

3. If a child is not vaccinated within four months after its birth, the public vaccinator of the district, after at least twenty-four hours' notice to the parent, shall visit the home of the child, and shall offer to vaccinate the child with glycerinated calf lymph, or such other lymph as may be issued by the local government board.

4. The public vaccinator shall not vaccinate a child if, in his opinion, the condition of the house in which it resides is such, or there is or has been such a recent prevalence of infectious disease in the district, that it cannot be safely vaccinated, and in that case shall give a certificate (under § 18 of the vaccination act of 1867) of postponement of vaccination, and shall forthwith give notice of any such certificate to the medical officer of health for the district.

5. Notwithstanding any regulation of any lying-in-hospital or infirmary, or other similar institution, the parent of any child born in any institution shall not be compelled under such regulation or otherwise to cause or permit the child to be vaccinated at any time earlier than the expiration of six months from its birth.

(II) 1. No parent or other person shall be liable to any penalty under § 29 or § 31 of the vaccination act of 1867, if within four months from the birth of the child he *satisfies two justices*, or a stipendiary, or metropolitan police magistrate, in petty sessions, *that he conscientiously believes that vaccination would be prejudicial to the child*, and within seven days thereafter delivers to the vaccination officer for the district a certificate by such justices or magistrate, of such conscientious objection.

2. This section shall come into operation on the passing of this act, but in its application to a child born before the passing of this act there shall be substituted for the period of four months from the birth of the child the period of four months from the passing of this act.

3. An order under § 31 of the vaccination act of 1867, directing that a child be vaccinated, shall not be made on any person who has previously been convicted of non-compliance with a similar order relating to the same child.

4. No proceedings under § 31 of the vaccination act of 1867 shall be taken against any parent or person who has been convicted under § 29 of the said act on account of the same child, until it has reached the age of four years.

5. Persons committed to prison on account of non-compliance with any order or non-payment of fines or costs under the vaccination acts shall be treated in the same way as first-class misdemeanants.

Italy.—Italy supports fourteen vaccine establishments, at Bologna, Milan, Genoa, Ancona, Venice (two), Bergamo, Arezzo, Verona, Vicenza, Rome, Modena, Ravenna, and Rimini.

A law of January 1st, 1892, provides for the production and preservation of vaccine lymph.

All children must now be vaccinated within the half-year succeeding their birth. Certain exemptions are specified—children who have had smallpox, etc.

Persons who have not been revaccinated since they were eight years old are excluded from schools and workshops until they are revaccinated.

Norway.—In Norway, vaccination was made obligatory by law in 1811.

In *Austria*, *Roumania*, *Turkey*, and in *Greece* the Government assumes the right to vaccinate all the unvaccinated, and in some of these countries to revaccinate all who have not been vaccinated within seven years. Vaccination is not compulsory in *Belgium* and in *Spain*.

In Vienna, Dr. Weyl attributes the low mortality from smallpox in the last years of the century to the introduction of the vaccination of school-children, to the active efforts of officials to arouse an interest in public vaccination, to the introduction of animal vaccine lymph, and to the establishment of a state institution for this purpose. ("Die Assanierung von Wien," 1902, p. 173.)

France.—After a century of failures to enact a compulsory vaccination law France has finally fallen into line by the enactment of a law which became operative in February, 1903. This act constitutes a portion of the new "law for the protection of the public health" of February 19th, 1902. It provides: (§ 6) that vaccination shall be obligatory during the first year of life, and also that revaccination shall be performed during the eleventh and twenty-first years. Parents and guardians are made responsible for the execution of this measure. A public regulation made after consultation with the Academy of Medicine and the Consulting Committee of Public Health will establish the necessary measures for carrying out the provisions of this act. By Article 23 the prefect of police is charged with the duty of enforcing the provisions of the act so far as penalties are concerned.[36]

Vaccination of all new recruits in the French army is obligatory, and to this regulation is undoubtedly due the comparative immunity of the army from smallpox as compared with the people at large.

Holland.—In Holland vaccination is not compulsory, and for many years it was the custom to delay vaccination until the child was more than two years of age.

There are at present four vaccine establishments, at Rotterdam, Amsterdam, The Hague, and Utrecht, and three temporary establishments at other places. Bovine lymph is mainly used at these.

Germany.—In Germany every child must be vaccinated in the year following the year of its birth. All scholars in public and private schools must be revaccinated in the twelfth year, if they have not already had the smallpox. When the vaccination and revaccination are not successful, they should be repeated in the two following years.

Only attested physicians may vaccinate. The special control of vaccination is left to the separate States. The public vaccinations are free to all. The cost is paid from the public treasury. Humanized lymph, retrovaccine lymph, and animal lymph may be employed indifferently. Humanized lymph is now scarcely ever used.

Dr. Wernher makes the just comment upon the age limit for vaccination that it is delayed too long for children, since children born in January may become twenty months old before their vaccination is obligatory.

Denmark.—Vaccination was established by law both in Denmark and in the Faroë Islands, at the beginning of the present century. By the laws of Denmark no child can be admitted to school, or present itself for confirmation, until a certificate of vaccination is produced. Revaccination is also enjoined for soldiers, and seamen in the navy.

In *Iceland*, which was subject to devastating epidemics of smallpox in the eighteenth century, one country physician and eight district physicians are appointed for the control of vaccination, and every clergyman, after having received the necessary instruction of these physicians, shall be the vaccinator *ex officio* of his parish and keep a register of those who are vaccinated. The district physicians provide a supply of vaccine virus from Copenhagen.

Sweden.—The law in Sweden prescribes, as a general rule, that children shall be vaccinated before the age of two years, and in case of epidemic smallpox vaccination is recommended in the first months of life. Revaccination is generally *recommended* at the age of fifteen years, and is *prescribed* for recruits in the army and navy.

Japan.—Vaccination was introduced into Japan in 1849 by Dr. Monnik, a Dutch physician at Nagasaki, and vaccinating offices were afterward opened; but the results were not at first satisfactory, in consequence of the want of a regular supply of good lymph and its deterioration, or on account of the imperfect performance of the operation. In June, 1874, a central office was opened for the purpose of collecting vaccine lymph from calves and distributing the same to the local authorities throughout the empire in the spring and autumn, and wherever smallpox should be prevalent.

In December of the same year (1874), vaccination was made compulsory, and regulations were issued for its performance and for the collecting of statistics relative to vaccination and revaccination.

Prof. E. S. Morse, who has been a keen observer of all matters of public interest in Japan, says: "It is gratifying to know that smallpox, which was formerly endemic, is now coming under control by the Government taking active measures to insure vaccination. The frightful scourges of smallpox in past times are seen in the sadly scarred faces of many of the people, and in the number of blind persons one encounters."

United States.—The following résumé contains the essential points of the vaccination laws of the principal States of the Union.

The following order of the Secretary of the Treasury relates to the vaccination of immigrants:

"Steerage passengers and crew, coming from districts where smallpox prevails in epidemic form, or who have been exposed to smallpox, shall be vaccinated before embarkation, unless they show evidence of immunity to smallpox by previous attack or recent successful vaccination."

In Alabama the county health officer is required from time to time to obtain necessary supplies of reliable vaccine matter which, without charge, he must, on application, furnish to the practising physicians of the county; and when prepared, vaccinate without charge all indigent persons of the county applying at his office.

Arkansas has no State law as to vaccination.

In California the law forbids the attendance of unvaccinated children at school, and it is provided that "any practising physicians may certify that the child or person has used due diligence and cannot be vaccinated so as to produce a successful vaccination, whereupon such child or person shall be exempted from the operation of the act" (Law of 1889).

In Colorado the local sanitary authority may provide for vaccination during the prevalence of smallpox, and even then only as an alternative to isolation.

In Connecticut the town boards of health may adopt such measures for the vaccination of the inhabitants of their respective towns as they deem necessary. Every person who refuses to be vaccinated, or prevents any one under his control from being vaccinated, on application of a member of a board of health, or of a physician employed by the board for such purpose (unless in the opinion of another physician it would not be prudent on account of illness), shall forfeit five dollars to the town.

The Board of School Visitors of any town has authority to require every child to be vaccinated before such child is permitted to attend a public school. The expense of vaccination is to be paid from the town treasury, when necessary.

In Delaware the school authorities are required to enforce the vaccination of all school-children, unless they are previously protected either by vaccination or by smallpox. A copy of the law must be posted for two weeks at the door of every school-house.

Florida.—By a law of 1889 the State Board of Health was authorized to make regulations. They made it the duty (by § 11 of the Sanitary Code) of city and town authorities to "provide for the vaccination and revaccination of the citizens residing in their several cities and towns." Every parent or guardian of a child is made responsible for its vaccination; exceptions were made in the case of sparsely settled districts when not threatened with smallpox, and in the case of a certificate from a reputable physician that vaccination would be "dangerous to the health of the person required to be vaccinated."

By §§ 12 and 13 superintendents of schools in towns having more than two thousand people, and owners or managers of factories are not to admit unvaccinated persons.

Illinois has no state law relative to vaccination. The State Board of Health has issued an order excluding unvaccinated children from the public schools and defines what it deems to be a "proper and successful vaccination."

Indiana has no state law as to vaccination. The State Board of Health has issued certain rules especially applicable to epidemic seasons. It has also ordered that bovine virus should be used for vaccination, with certain exceptions.

In Iowa the attendance of unvaccinated children at school is forbidden.

In Kansas there is no state law as to vaccination.

In Kentucky the law requires that all unvaccinated persons over twenty-one years of age shall procure their own vaccination. Parents and guardians must have their children and wards vaccinated within twelve months after their birth. The secretary of the State Board of Health is required to furnish vaccine virus to local boards of health for the gratuitous vaccination of the poor.

Louisiana has no state law as to vaccination. A city ordinance relative to school attendance is enforced in New Orleans.

In Maine the city or town authorities are required annually, or oftener if they deem it prudent, to provide for "free vaccination with the cowpox" of all inhabitants over two years of age, to be done under the care of skilled practising physicians, under such circumstances and restrictions as the authorities may adopt. School committees may, if they deem it expedient, exclude unvaccinated children from the public schools.

A law was enacted in Maine in 1889 providing for the

exclusion of all unvaccinated persons from paper mills, where domestic or foreign rags are used, under penalty of fifty dollars or less.

In Maryland, a state vaccine agency is established which is required to keep a supply of fresh vaccine virus for the use of physicians. The governor is required to appoint a vaccine agent with prescribed powers and duties. Physicians are authorized to vaccinate children born in their practice. A penalty is provided for the use of virus of bad quality. Parents are charged with the duty of having their children vaccinated within twelve months after their birth. Unvaccinated children are not to be admitted to the public schools. Small fruit-growers, canners, truck farmers, and fish-packers must not employ persons who do not show written proof of vaccination of more recent date than July, 1898. Penalty, $50 to $500 (order of State Board of Health of March 6th, 1899).

In Massachusetts the law provides that parents and guardians shall cause their children and wards to be vaccinated before they attain the age of two years, and revaccinated whenever the town authorities shall, after five years from the last vaccination, require it. The town authorities shall also require and enforce the vaccination and revaccination of all inhabitants when the public health requires it. The penalty for neglecting to comply with these provisions is $5. Towns shall furnish means for vaccination to those who cannot pay for it. Incorporated manufacturing companies and superintendents of public institutions are required to see that the inmates of such institutions are vaccinated. Towns may make further provisions for vaccination, under the direction of the Board of Health, or of a committee chosen for the purpose. School committees are required to exclude unvaccinated children from the public schools, except "any child who presents a certificate signed by a registered physician designated by the parent or guardian, that the physician has at the time of giving the certificate personally examined the child, and that he is of the opinion that the physical condition of the child is such that his health will be endangered by vaccination, shall not, while such condition continues, be subject to the provisions of" the vaccination acts (chap. 190, Mass. Acts of 1902).

In Michigan townships may make suitable provision for the "inoculation of the inhabitants with the cowpox," under the direction of the Board of Health, or of the health officer. The Board of Health of each municipality may at any time direct its health officer or physician to offer vaccination with bovine vaccine virus to every child not previously vaccinated, and to all other persons not vaccinated within the preceding five years. Any health officer is also authorized to order the prompt vaccination or isolation of persons who have been exposed to smallpox.

In Minnesota parents and guardians are charged with the duty of having minors vaccinated.

Missouri has no state law as to vaccination.

In New Hampshire the law is permissive as to the appointment of agents for the vaccination of towns. Unvaccinated children are excluded from the schools.

In New Jersey the school authorities may prohibit the attendance of unvaccinated children who have not had the smallpox, and may decide whether revaccination shall be required when smallpox occurs in any city or district. In the enrollment of children by the school authorities, inquiry must be made as to the fact of vaccination, and if the parents desire, children are to be vaccinated by a regularly licensed physician. The State Board of Health may prohibit the manufacture and sale of impure vaccine virus, antitoxin, or other animal product (Law of 1895).

In New York it is the duty of local boards of health to provide at stated intervals supplies of vaccine virus, of a quality and from a source approved by the State Board of Health. During an epidemic, local boards of health are to obtain fresh supplies of virus, at intervals not exceeding one week, and at all times to provide thorough and safe vaccination for all persons who may need it.

In North Carolina cities, towns, and counties may make rules requiring vaccination (Law of 1893).

In Ohio local boards of health may take measures, supply agents, and afford inducements and facilities for gratuitous vaccination. They may also make and enforce such rules and regulations to secure the vaccination of school-children as in their opinion the safety and interests of the people require.

In Pennsylvania by a law of 1895 the Bureau of Health may issue an order requiring all persons in a city, or any part thereof, to be vaccinated within such time as the Bureau shall prescribe. Penalty, $5 to $20.

Unvaccinated children may be refused admission to school.

In Rhode Island the town councils shall provide annually for the gratuitous vaccination of the inhabitants. They shall also contract with and provide physicians to vaccinate. Such physicians are to record the names and ages of persons vaccinated. Unvaccinated children are excluded from the public schools. The maximum fine for violation of the law is $50, or imprisonment for thirty days.

In South Carolina the State Board of Health may order vaccination (Chap. 77, Laws of 1899).

In Tennessee the State Board of Health has power to prescribe rules to prevent the introduction of epidemic diseases.

In Vermont, by a law of 1892, the local board of health must provide, whenever it is deemed necessary by the State Board of Health, a suitable supply of vaccine virus of a quality and from a source approved by said State Board of Health; and during the existence of an actual outbreak of smallpox in any town or city, the local board of health shall at all times provide thorough and safe vaccination for all persons within its jurisdiction who may need the same.

In Virginia unvaccinated children are excluded from the public schools. The governor is required to appoint an agent annually, who must furnish, by mail or otherwise, to every citizen of the State who applies for it, genuine vaccine virus, free of charge, with directions how to use it. The agent must advertise that he is ready to furnish such virus. The town and city authorities may cause the inhabitants to be vaccinated, and may enforce obedience by fixing fines and penalties for violation.

West Virginia also had a statute requiring the appointment of a vaccine agent, but this has recently been repealed.

In Wisconsin the following remarkable decision of the courts is published:

"Compulsory vaccination as a condition precedent to school attendance cannot be sustained as an exercise of police powers by the Board of Health in the absence of a statutory provision requiring it.

"If the Board of Health possessed the power to make a rule excluding children from the public schools without a certificate of vaccination, it is void as unreasonable when no epidemic, and but a few scattered cases of smallpox exist in the State where the rule is adopted, and but one case in the city where adopted, and that quarantined" (Adams v. Burdge, 95, 390, Wisconsin).

ANTIVACCINATION. — Vaccination, like almost every important discovery which has ever been made, has had its opponents from the very outset.

The literature of antivaccination is quite considerable, and consists of many pamphlets in English, the principal writers being Messrs. Gibbs, Tebb, Taylor, Young, Wilkinson, and Prof. A. R. Wallace. Several journals devoted to the same cause are published in English, the *Vaccination Inquirer* being the organ of the first-named society.

There are also many continental pamphlets upon the same subject, chiefly in French, German, and Swedish.

The most decided resistance to the vaccination acts in England has been for several years in the county of Leicester, where the number of unvaccinated children has

increased during the past few years until, in the returns for 1896, it appears that the neglect of vaccination amounted to 79 per cent. of the births, and in the city it amounted to 82.1 per cent.

The following figures show the increasing neglect in regard to vaccination, both in London and in the whole country:

PROPORTION NOT FINALLY ACCOUNTED FOR IN REGARD TO VACCINATION.

Year.	London.	Rest of England.	Year.	London.	Rest of England.
1887	9.0	6.7	1894	20.6	19.0
1888	10.3	8.2	1895	24.9	19.8
1889	11.6	9.6	1896	26.4	22.3
1890	13.9	10.9	1897	29.1	21.6
1891	16.4	12.9	1898	33.0	19.6
1892	18.4	14.3	1899	27.7	15.4
1893	18.2	15.7			

Dr. Arnould, in his treatise on "Public Hygiene," recognizing the fact that an unvaccinated person is a constant menace to the public safety, reasonably inquires whether the *liberty* of those who do not wish to have the smallpox is not as worthy of respect as the *liberty* of those who do not desire to be vaccinated.

In France, the opponents of compulsory vaccination succeeded in preventing the enactment of the bill proposed by Dr Liouville, in 1881; and in Switzerland a similar organized opposition secured the repeal of compulsory acts in 1882, the effect of which action very soon became evident in a decided increase of smallpox in that country.

The opposition to vaccination is based mainly upon the following objections:

1. Alleged infringement of personal liberty. Upon this subject, Dr. J. M. Toner, of Washington, makes the following excellent comments:

"The question of the prophylactic power and safety of vaccination is so well settled that the individual who fails to protect himself against variola by it should be looked upon by the community with aversion, and treated as a nuisance (as he really is, so far as the social interests are concerned), and be compelled to submit to vaccination for his own safety and the protection of the public.

"Parents and guardians have no more right to withhold or neglect to provide vaccination for the children under their protection than they have to jeopardize the lives of their helpless infants by not furnishing them with food or clothing. It is criminal to neglect either, as death may be the consequence; but the failure to provide protection against smallpox seems to be more maliciously wicked than to neglect either food or clothing, as the former may not only cause the death of the child, but may be the means of spreading disease and death among many others; while the evil which arises from the latter ceases with the death of the victim."

2. As to the claim that vaccination does not protect from smallpox.

The amount of protection afforded by the process of vaccination, when properly performed, has been quite fully discussed in the earlier portion of this article. At the present day, but very few authorities claim that the protection afforded by a single vaccination is absolute. Not even smallpox itself is protective in all cases against a second attack. The amount of protection afforded is quite well shown by the statistics of epidemics. Dr. Buchanan, medical officer of the Local Government Board of England, showed that the smallpox death rate among adult persons vaccinated was 90 to the million; among the unvaccinated it was 3,350 per million. Among vaccinated children under five years age it was 40.5 per million; among unvaccinated children of the same age it was 5,950 per million.

3. As to the claim that vaccination introduces other diseases besides vaccinia. As has already been stated, the fact that such cases have occurred is not denied. It is also true that cases of such injury are exceedingly rare. So far as the introduction of diseases of human origin is concerned, this objection is entirely overcome by the employment of bovine virus; and with reference to the possibility of introducing any of the diseases common to the cow and to man, the question has been sufficiently answered by the quotations already given.

With reference to the various incidents which occasionally follow vaccination, very much has been attributed to the operation which does not belong to it, on the entirely erroneous principle of *post hoc, ergo propter hoc*. The mortality from all causes among children is large, and in a large number of annual vaccinations, as for example, among the two millions or more of the German Government, it is not remarkable that a considerable number of deaths should occur within a short period of vaccination, and cases of harm are attributed to the operation which actually have no connection with it, in the line of cause and effect.

4. A singular argument often urged by the opponents of vaccination is, that smallpox is not caused by contagion, but by filth, and hence its proper preventive treatment should be accomplished simply by sanitary measures, without vaccination. Undoubtedly, filth and bad hygienic conditions promote the spread of smallpox, but that they directly cause the disease in the absence of a previous case of smallpox has never been proven. On the other hand, the disease has been shown to be contagious and inoculable in the highest degree.

With reference to the theory of the origin of smallpox from filth, Dr. Carpenter says: "As regards smallpox, there is not any difference of opinion on this point. It certainly requires the introduction from without of some form of particulate contagion (a germ or living organism), however much meteorological states and personal diet may promote its growth; and if the contagion be absent, smallpox cannot arise."

5. Displacement of mortality (Carnot's doctrine). This theory was proposed by M. Carnot, a French artillery officer. He alleged that, while certain diseases, such as smallpox, measles, convulsions, and croup, were decreasing, other diseases, such as cholera, typhoid fever, and dysentery, were increasing; that the births were tending to become less in number than the deaths; that the depopulation of France was an imminent danger; and that vaccination was the cause of all this disturbance. Mr. Simon comments upon this remarkable theory as follows: "Supposing Carnot's statistics to be correct, does he give any sufficient reason for ascribing to vaccination that deteriorated state of adult life which he professes to have discovered? So little does he this, that in any of the sentences where damnatory conclusions are drawn, if there were substituted at hazard for his word *vaccination*, the mention of any other historical event belonging to about the same period of time as Jenner's discovery, M. Carnot's logic would scarcely suffer by the change, or his new conclusion be less warrantable than his first. *Post ergo propter* was never more whimsically illustrated. For the argument goes simply to claim as the *effect* of vaccination whatever evils have occurred since its discovery; and M. Carnot's moderation may be praised, that, with the infinite resources of this proof, he did not also convict Jenner of causing last year's inundation of the Rhone."

M. Charles Dupin, in 1848, and Dr. Bertillon, in 1854, also exposed the fallacy of Carnot's proposition. It was shown that, whether his arithmetic were right or wrong, his medical conclusions were wholly untenable. His evidence was purely local and applied to France, in which there were, it is true, certain facts of an unfavorable character relative to the growth or movement of the population; and yet these same observations were not applicable to England, nor to Sweden, nor to Russia, nor to any other countries in which vaccination was practised as well as in France.

Has Vaccination Increased the Liability to Other Diseases, and has it Increased the General Death Rate?—

Both of these propositions have been advanced by the opponents of vaccination. Let it first be inquired what is meant by these propositions.

"A child whose liability to smallpox has just been extinguished by well-performed vaccination," says Simon, "may to-morrow, like an unvaccinated child, be run over, or be drowned, or become sick of measles, or suffer with teething, or be struck with any other of the numberless shafts of death. And the vaccinated subject, advancing to adolescence, to middle life, or to old age, must encounter, like the unvaccinated, the several risks of each period of life. And obviously, if vaccination on a given day, in England, secures a thousand lives from death by smallpox, sooner or later those lives will be subject to the inevitable lot; sooner or later the thousand deaths will be written against the names of other diseases than smallpox; and such diseases may then be said to have been rendered more frequent by vaccination. In the same sense every life that is snatched from fire, or flood, or poison counts at last as a death from some other cause; and to say *in this sense* that such causes are more fatal than before vaccination, is but another form of saying, what Jenner would most have wished to hear, that smallpox is less fatal than it was."

Dr. W. Channing relates a case of a young mother who desired to have her child vaccinated, but hesitated and declined to have it performed. In a few days the child was covered with a loathsome eruption. Had vaccination been performed, the disease would undoubtedly have been attributed to the operation (*Boston Medical and Surgical Journal*, March 1st, 1860).

The British Parliamentary Commission of 1889.—From the very beginning of the introduction of vaccination opposition has been manifested to its practice, the degree of resistance differing much in different countries. In England several parliamentary inquiries have been held upon the subject, the general result of which has been a confirmation and strengthening of existing laws upon vaccination. The last Parliamentary Commission appointed to consider this subject was that of 1889. The commission consisted of fifteen members, of which Lord Herschel was chairman. Several voluminous reports of this Commission were published containing an enormous amount of evidence together with many appendices containing valuable information, covering about 3,300 folio pages of closely printed matter. Many witnesses were examined by this commission, including such noted experts as Sir John Simon, Dr. Ogle, of the Registrar-General's Office, Dr. Buchanan, Dr. Thorne Thorne, Dr. Cory, Dr. Barry, and other officials of the Local Government Board of England. The principal advocates of repeal of the compulsory laws were Alfred Russell Wallace, LL.D., Messrs. Alexander Wheeler, William Tebb, and others.

The points which this commission was charged to consider were the following:

1. The effect of vaccination in reducing the prevalence of, and mortality from, smallpox.

2. What means, other than vaccination, can be used for diminishing the prevalence of smallpox, and how far such means could be relied on in place of vaccination.

3. The objections made to vaccination on the ground of injurious effects alleged to result therefrom; and the nature and extent of any injurious effects which do, in fact, so result.

4. Whether any, and if so, what means should be adopted for preventing or lessening the ill effects, if any, resulting from vaccination; and whether, and if so, by what means, vaccination with animal vaccine should be further facilitated as a part of public vaccination.

5. Whether any alterations should be made in the arrangements and proceedings for securing the performance of vaccination, and, in particular, in the provisions of the Vaccination Acts with respect to prosecutions for non-compliance with the law.

The commission made an interim report April 21st, 1892, at which time it had held ninety meetings and examined one hundred and thirty-five witnesses. The final report was not made until 1896. The two recommendations which the commission made in its interim report were substantially as follows:

1. It appears that the courts had so construed the laws as to warrant repeated orders in respect to the non-vaccination of a child and the imposition of a penalty for the disobedience of each of such orders, notwithstanding that previous penalties have been inflicted. The commission agreed that the imposition of repeated penalties in respect to the non-vaccination of the same child should no longer be possible. They arrived at this conclusion independently of the question whether vaccination should continue to be compulsorily enforced.

Those who favored the view that vaccination ought not to be compulsory were naturally opposed to repeated convictions; while those who inclined to the opposite view believed that any advantage which could arise from the tendency of repeated convictions to increase the number of the vaccinated, is more than counterbalanced by the resentment and active opposition to vaccination which they engender.

2. The question having arisen whether a person committed to prison on account of failure to pay the penalty imposed under the Vaccination Laws, should be treated as a criminal or not, the commission expressed its opinion that such persons "should no longer be subjected to the same treatment as criminals. Many of the victims of such imprisonment regard the practice of vaccination as likely to be injurious to the health of their children, and are well-conducted and in other respects law-abiding citizens. Even those who consider that the course which such persons adopt is a mistaken one may nevertheless well be of the opinion that they ought not, during their imprisonment, to be subjected to the treatment awarded to criminals, such a proceding not being calculated to secure obedience to the law or to add to the numbers of the vaccinated."

Dr. Alfred Russell Wallace appeared before the Royal Vaccination Commission, in 1890, as a convert to the principles of anti-vaccination, and was hailed by the opponents of vaccination with great triumph. Dr. Wallace confidently expected to demolish the arguments in favor of vaccination upon scientific principles, and appeared before the commission with a long array of tables of statistics and diagrams which fill many pages in the third report of the commission. The principal part of these statistics relates to vaccination in the departments of France for a period of about twenty years. The data presented for each department are the number of births, number of vaccinations, and number of deaths from smallpox for each year, the object being to show that vaccination increases smallpox.

These tables were taken up and carefully considered by the commission, and, so far as Dr. Wallace's hasty conclusions were concerned, they were found to be worthless. This witness finally admitted, after retreating step by step, that his tables were "not perfect," that "the imperfection is very great and irregular." He also admitted that, if his entry of "no deaths" often meant nothing more than that there had been "no returns" (which was actually the case), "then, of course, the whole thing is imperfect," and that in view of such a defect, which was vitally important, "the whole thing is valueless."

Criticism followed upon criticism, and at last Dr. Wallace asked that he might make a few personal concluding remarks, the pith of which had to do with suggestions from the commission that he must have "taken up this subject and written upon it without full and accurate information befitting a man of science." And, in making the personal explanation, the previous declarations as to the absolute need for a scientific accuracy such as had controlled the labors of Darwin seems to have been forgotten, and in their place came the frank admission, "My answer is that I did not take it up as a question of pure science."

Thus ended the "absolute test and demonstration" held out at the previous session of the commission, and

the result is that the opponents of vaccination still lack a scientific statistician as an exponent of their views (editorial in *Practitioner*, 1891, vol. xlvi., p. 465).

The smallpox statistics of Prussia, which Dr. Wallace presented to the commission, were brought down to the year 1874, and there discontinued. The compulsory law of Prussia was enacted in 1874, and Dr Wallace admitted that "he had heard of it," but had not seen any evidence that it made any important difference.

On the contrary, there are nowhere to be found any statistics so absolutely conclusive of the value of vaccination as the comparative statistics of Prussia for the two periods before and after the enactment of the compulsory vaccination law of 1874.

The London *Lancet*, in commenting upon the testimony of this witness, says that Dr. Wallace's theory was based upon "blunders that would hardly be expected of a school boy," and in a concluding paragraph upon the same subject affirms, "if this is all that science can do for the antivaccinationists, the scientific value of vaccination stands more than ever confirmed." But, notwithstanding the exposure of his errors, the philosopher obstinately adheres to his position that "vaccination is a delusion" ("The Wonderful Century," New York, 1899). In this paper he quotes largely from the experience of English towns in which vaccination is only partially enforced, and utterly ignores the greatest and best example of modern times—the German nation. He also quoted the experience of Leicester, England, but takes special pains to omit all reference to the difference between the smallpox mortality of the vaccinated and the unvaccinated in that city, as shown so clearly by its medical officer, Dr. Priestly, in his report of the epidemic of 1892–93. Out of a total of twenty-one deaths from smallpox in that city nineteen were those of unvaccinated persons, one had been vaccinated and the facts in regard to the remaining one were unknown.

The principal modern opponents of vaccination who have published their views upon the subject are Prof. E. M. Crookshank, Dr. Charles Creighton, Professor Wallace, Mr. William Tebb, Prof. A. Vogt, of Berne, and Lorinser, of Vienna.

The final outcome of this legislative farce was the enactment of the "conscientious objector" clause already quoted. The practical operation of such a law is sufficiently illustrated in the following report of the first case which came to trial January 27th, 1899:

The First Appeal Under the Vaccination Act, 1899. Regina v. Welby, ex-parte Bird, January 27th, 1899.—The absurdity of the provisions of § 2 (1) of the Vaccination Act, 1898, which require that the parents or person responsible for having a child vaccinated must "satisfy" the magistrate before whom he is brought, that he "conscientiously believes that vaccination would be prejudicial to the health of the child," in order to escape liability to a penalty under § 29 or § 30 of the Vaccination Act, 1867, was fully demonstrated in the above case, which formed the ground of the first appeal under the section.

One Walter Bird had endeavored to "satisfy" the stipendiary magistrate of Sheffield as to his child, as required by § 2 (1) of the Act, but failed to do so. Being convinced that the stipendiary ought to have been "satisfied," he applied for and obtained a rule from the court of Queen's Bench (the Lord Chief Justice and Mr. Justice Wills), calling on the stipendiary to show cause why a *mandamus* should not issue directing him to hear and determine the case, as he had declined to grant exemption to the child on the ground that he did not believe that Bird conscientiously believed that vaccination would be injurious to the child.

In granting the rule the Lord Chief Justice said, *inter alia*:

"The section clearly said that the magistrate was to be satisfied, not in his opinion that vaccination would be prejudicial to the health of the child, but satisfied that the applicant conscientiously believed that vaccination would be prejudicial to the child."

When the case came on for hearing before the Divisional Court (Lawrence and Channell, J. J.), after the affidavits of the parents had been read and explained by counsel, who stated that the parents had been prosecuted and had suffered great inconvenience, Channell, J., said: "The magistrate said in his affidavit, 'A certificate was not given because I was not satisfied that he believed that vaccination would be prejudicial to the health of the child.' They could not grant a *mandamus* to compel him to be satisfied. . . . He has to satisfy the magistrate of his belief, and he has not done so. Even if the magistrate is wrong, we cannot make him be satisfied."

The rule was discharged (Himes' "Handy Guide to the Public Health Acts," London, 1901).

Dr. Creighton's views upon vaccination are sufficiently set forth in his article in the twenty-fourth volume of the "Encyclopædia Britannica," and in his book entitled "Cowpox and Vaccinal Syphilis." In the former he takes the ground that there is neither identity nor even affinity between vaccinia and variola. He also asserts his belief that the diminished activity of variola is due to epidemiological laws, and not to vaccination. In his exceedingly superficial statement of the practical working of vaccination laws, like Dr. Wallace, he omits reference to the convincing experience of Prussia since the enactment of more efficient laws in 1874, although a dozen years or more had elapsed from that date to the publication of his article in the "British Encyclopædia."

The various publications issued by the opponents of vaccination are characterized mainly by the absence of facts and the presentation of an abundance of theory. For example, a recent work by Mr. William Tebb, intended to prove the "synchronicity between the spread of leprosy and vaccination," introduces many arguments in support of an alleged connection between the one and the other. But leprosy produced its most disastrous effects in the twelfth, thirteenth, and fourteenth centuries, when vaccination was unknown. There were then nineteen thousand lazarettos in Europe. Now that the human race is much more widely distributed over the globe, leprosy is far more rare, and exists to its greatest extent in countries where vaccination is but little practised. In the United States, where probably more than three-fourths of the population is vaccinated, leprosy is confined chiefly to a very small number, among whom the disease was introduced directly from other and infected countries.

Leprosy has for many years been prevalent in Bombay, but since the introduction of vaccination there, by the British Government, the ratio of lepers has gradually diminished.

Much importance has been attached by the opponents of vaccination to certain statistics which were published in 1872–73 by Dr. Keller, the chief physician of the Austrian State Railway, who was himself an opponent of vaccination. These statistics were quoted largely by Lorinser of Vienna, Vogt of Berne, and by Reichsperger, all of whom were antivaccinationists. Körösi recently investigated the sources of these statistics, and ascertained that Keller was dead, and that the original documents could not be found. He then corresponded with all of the physicians who had contributed material to these statistics, who were still living and could be found, and learned that not only had Keller suppressed important data, but had actually altered the returns to suit his own views. One of the physicians who contributed to the returns confessed that "the data were prepared in conformity to the taste of their chief, whom he knew to be opposed to vaccination."

The committee of the Ninth International Medical Congress who examined the proofs of these statements reported that they were "forced to declare that the statistics of Dr. Keller were found to be false; that they are an unpardonable effort to mislead public and scientific opinion, and that henceforth no weight should be attached to them, having been proved by us to be entirely incorrect."

Samuel W. Abbott.

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VAGINA, ANATOMY OF. See *Sexual Organs, Female.*

VAGINA, CONGENITAL MALFORMATIONS OF THE.—DEVELOPMENT OF THE VAGINA.—A knowledge of the mode in which the vagina is developed is essential to a proper understanding of its congenital malformations.

The lower portions of the two Müllerian ducts coalesce to form the vagina, and by the ninth week of embryonal life the intervening septum disappears, and this union is complete, although the appearance of the cervix and the differentiation of the genital passage into uterus and vagina cannot be said to take place before the fifteenth or sixteenth week. In the nineteenth week of fœtal existence a slight projection of mucous membrane makes its appearance on the posterior wall of the entrance to the genitalia, just above the point of union of the vagina with the urogenital sinus, and a little later a smaller projection at a slightly higher level may be seen on the anterior wall. These elevations subsequently unite laterally, and thus form the hymen, which, by the twentieth week, is fully developed.

VARIETIES OF CONGENITAL MALFORMATIONS.—The vagina may be entirely absent; it may be more or less completely closed by a transverse, or divided by a longitudinal, septum; though not seriously misshapen it may still be too short or too narrow; or it may communicate with cavities from which it should properly be separated. There are yet other errors in development, which are, however, of less import.

A. *Absence of the Vagina.*—When there is total failure in development of the lower portions of the ducts of Müller the vagina is entirely absent, and only a thin septum intervenes between the bladder and the rectum, in which some little connective tissue, but no muscular elements, are discoverable. A fibrous strand or cord may, however, indicate the situation which should be occupied by the vaginal tube. When the Müllerian ducts are developed, except at their very lowest extremities, or are not prolonged downward far enough to open into the aditus urogenitalis, then only the most inferior portion of the vagina is wanting.

Absence of the vagina is usually associated with some other marked maldevelopment, such as absence or a rudimentary condition of the uterus. The condition of the uterus will determine the existence or non-existence of retained fluids.

In absence of the vagina the urethra is found to be abnormally relaxed.

If there is hæmatometra, an operation designed to create a passage where the vagina should be located is imperative; and even when only a very rudimentary uterus can be discovered, and there is no retention, the general health of the individual is often markedly improved after operative interference is instituted, and the uterus has been known to take on active growth.

When there is sufficient space between the bladder and rectum, a vagina can be made by stretching and tearing the intervening tissues with the finger, aided by the use of blunt-pointed scissors, if great resistance is encountered.

A sound in the urethra, and the finger of the operator or of an assistant in the rectum, are useful guides. The operation should be completed at one sitting, and the passage should be made larger than it is thought desirable to have it subsequently remain. Undue contraction is prevented by the use of a vaginal plug of glass, and the cicatricial tissue which forms over it is said to resemble very closely normal mucous membrane.

When the uterus is well developed, and there is retention, but no vaginal passage can be formed, Battey's operation may be indicated.

B. *Atresia of the Simple Vagina.*—In this condition the occlusion of the vagina is absolute. The obstruction may be seated at the hymen—atresia hymenalis, or at some point within the vagina proper—atresia vaginalis.

Atresia Hymenalis.—Atresia hymenalis is the most common variety of vaginal atresia. The duplicature of mucous membrane constituting the hymen here forms an obstruction, which, although thinner and more elastic than the atresias situated above in the vagina, yet may

be considerably thickened and of almost cartilaginous toughness. As menstrual blood accumulates, the hymen bulges downward, and the vagina dilates above, until it forms a sac filling the pelvic cavity. The uterus at first is undisturbed, and rests upon the summit of the distended sac. Ultimately the cervix, and even the uterus, if no outlet is found below, become dilated. The tubes likewise suffer, but the blood discovered in them is by some not regarded as an overflow from the uterine cavity, since the uterine ends of the tubes are often closed, and the blood is located in small diverticula or sacs near the fimbriated extremities, and is said to originate in hemorrhages from the mucous membrane of the oviducts themselves. The blood may, however, subsequently escape into the peritoneal cavity from the fimbriated ends of the Fallopian tubes.

Atresia Vaginalis.—In atresia vaginalis the obstruction (or obstructions, for there may be several, located one above the other, and separated by layers of different kinds of retained fluid) is generally found in the lower third of the vagina. The thickness of the atresia varies in different cases, and whatever may have been its original dimensions, pressure from the fluid accumulation above produces sometimes a remarkable degree of thinning. Thus the obliteration may be 1.2 inch thick, or of membrane-like delicacy. In atresia vaginalis, however, we do not find the elasticity and distensibility met with in atresia hymenalis. The occluding membrane, made up largely of connective tissue, is of a firmer texture and greater thickness, and yields less readily beneath the superincumbent weight. As a result of this, the lower part of the vagina and the vulvar orifice are seldom dilated, and the former is not uncommonly narrow and cone-shaped, although attempts at coition may materially modify its shape, while the occluding diaphragm viewed from below may appear quite flat.

It is very important, in view of proposed operative interference, to ascertain the seat and thickness of the occluding membrane, and this is best done by the various combined methods of examination, a catheter or sound placed in the bladder being employed to assist the finger in the rectum or vagina.

Above the obstruction, as in atresia hymenalis, mucus or blood accumulates. The seat of the atresia, and the activity and frequency of the menstrual function, determine largely the quantity of the accumulated blood; but, as has been pointed out, nature, discovering an obstacle to escape, retards in some way the amount of blood effused, so that it is never as great as one would expect to find it, considering the number of periods that have occurred, and is always less in congenital atresia than in the acquired condition. It is probable, also, either that the uterus is in an immature and inactive condition, or else that the fluid elements of the accumulated blood have been largely absorbed. The peculiar characteristics of the retained liquid would seem to support this last assumption, for it is found to be dark reddish-brown in color, and of a thick, tenacious consistence, the mucus mingled with it preventing coagulation.

Microscopically it is found to contain shrivelled blood corpuscles, and extravasated blood pigment, with flat epithelial cells, mucous corpuscles, and granular débris.

As in atresia hymenalis, the genital tube above the point of obstruction dilates as the retained fluid accumulates. At first the vagina, then the cervical canal, and finally the uterine cavity become filled and expand often to a remarkable degree; the distended vagina will, however, always constitute the major part of the tumor. If the liquid is mucus, the conditions known respectively as hydrocolpos and hydrometra develop; if blood, then the terms hæmatocolpos and hæmatometra are employed. Fortunately, the walls of the dilated portion of the vagina, although overstretched, do not become thinned. On the contrary, they hypertrophy, especially their musculature, and the condition known as "excentric hypertrophy" is thus developed.

The vaginal walls internally may be thrown into folds, although the sac be greatly distended. Occasionally, in new-born children, the folds of mucous membrane on opposite walls of the vagina become united, forming a thin, transparent diaphragm, which soon ruptures spontaneously, and is seen no more.

The origin of the obstruction in atresia hymenalis has been variously explained. It is said that the fusion of the lower ends of two solid Müllerian ducts will produce this abnormality, or that there may be an overgrowth of the fold of mucous membrane which constitutes the hymen and a union of its free edges toward the centre of the ring. Fœtal inflammation may likewise produce an agglutination of these same free edges after the hymen has been completely formed. Numerous hypotheses have likewise been advanced to explain the origin of atresia vaginalis. Either the lumen of the vagina at some point has never been established, as when the Müllerian ducts as solid cords have united, but have failed to become hollowed or tunnelled at the point in question; or else, after a normal formation of the vagina by proper coalescence and perforation of these ducts, its walls, for a variable distance, become united one with the other, as the result of an inflammation during intra-uterine life. And further, the idea has been suggested that, in cases in which there is but one septum, the canal above the septum may belong to one Müllerian duct and that below to the other. In explanation of the fact that atresias are most often seated in the lower third of the vagina, it should be borne in mind that the walls of the vaginal tube are very closely approximated just above the seat of the hymen, and agglutination is thereby rendered easy.

Atresias of the vagina are important only as interfering with menstruation and coition. Hence, although exceptionally before puberty these occlusions may give rise to inconvenience or suffering (as in certain cases of profuse secretion of mucus and the formation of a hydrocolpos, a condition rarely of significance in adults), yet in the majority of cases it is not until the establishment of the menstrual function, and, more rarely, when graver rudimentary conditions exist and the catamenia do not appear, not until after marriage, that symptoms manifest themselves and a physician is consulted. Certain well-known general conditions may likewise postpone the ushering in of the first menstrual period, and then if an accumulation occur it will be of mucus and not of blood.

In atresia of the hymen or of the vagina proper, when puberty arrives the usual disturbances which precede and accompany the catamenia are noticed, but there is no discharge. At the time of the next period these disturbances are somewhat accentuated, and, as the fluid accumulates, gradually change to suffering, which is experienced now during the intermenstrual period as well. The tumor produces pain and a feeling of weight in the pelvis, and by pressure or traction upon the bladder and rectum interferes with micturition and defecation. There is sometimes, too, no little constitutional disturbance. The amount of fluid and the consequent size of the tumor determine in large part the intensity of suffering, which is also influenced by the general condition of the patient.

Usually, after menstrual molimina have been noticed for three successive months, a tumor begins to be apparent, although it may not be noticed until a much later period, and this swelling gradually enlarges until it bulges at the vaginal inlet and causes a perceptible increase in the size of the abdomen. Certain conditions previously described may, however, retard its development, and the sac may never attain very great proportions.

If menstruation has never appeared and the accumulation of mucus has not been excessive, it may be that futile or unsatisfactory attempts at intercourse first reveal the existence of an atresia. Yet if the atresia be elastic or high-seated, repeated efforts at cohabitation ultimately form a fairly roomy canal, or, if the diaphragm be low or unyielding, intercourse may be carried on through the urethra or anus. It is extraordinary how greatly the urethra may become dilated under these cir-

cumstances, and it is still more singular that incontinence of urine so seldom results Occasionally sterility first induces a patient to seek medical advice.

Spontaneous rupture of the occluding membrane and evacuation of the retained fluid are rare in both forms of vaginal atresia; they occur in only one per cent. of cases of atresia vaginalis. And, indeed, although a source of temporary relief, this natural effort at cure is of somewhat questionable value. Pyocolpos and pyometra almost invariably result, and the danger to the patient is, if anything, aggravated. Yet if spontaneous perforation does not occur, and no surgical procedure looking to the emptying of the sac is instituted, the outlook is extremely unfavorable. Rupture of some portion of the distended genital tube, or of a blood sac in the oviduct, is almost sure to occur, or else without rupture a grave peritonitis may develop.

The symptoms observed at puberty, and repeated periodically afterward, which have already been detailed, are quite characteristic, and, with the accompanying physical signs of a gradually increasing retention tumor, leave but little doubt as to the diagnosis. It is true that amenorrhœa and abdominal enlargement may, and sometimes do, give rise to the impression that pregnancy exists, but this is rapidly dispelled by a local examination and a careful inquiry into the history of the case. In view of the serious nature of the malformation in question the physician is justified in insisting at least upon an examination of the rectum and abdomen, if not of the genitals, in all doubtful cases. And this examination should be undertaken early and be performed carefully; for although the recognition of a vaginal atresia is a matter of no great difficulty, yet it is not always easy to determine the exact seat, and more especially the thickness, of the obstructing membrane, which are matters of great importance when surgical interference is attempted.

The various combined manual and digital methods of exploration are the means generally employed, and a sound or catheter of some resistant material, placed in the bladder, often assists in arriving at a definite opinion. In children the persistence of dysuria may, after simple remedies fail, suggest the necessity for an examination; and in adults dyspareunia and sterility, in a case in which menstruation has never occurred, likewise require investigation. To differentiate between atresia hymenalis and atresia vaginalis is not always so easy as one would suppose. In atresia hymenalis, if there be retention, the sac distends the perineum and protrudes from the vulvar orifice. The obstruction in atresia vaginalis is thicker and less elastic, and there is not so much likelihood of distention of the lower vagina and separation of the vulvar fissure; but if it be seated, as is usual, in the lower third of the vagina, the sac may bulge through the genital outlet, the hymen being seen adherent to it like a fringe. However, in atresia vaginalis the lower part of the vagina is often narrow and cone-shaped, and the diaphragm itself may appear flat. Atresias of the vagina which are located at a higher level are more difficult to delimit accurately, but are less likely to give rise to confusion with imperforate hymen.

It is not always easy in a given case to decide whether an atresia is congential or acquired. Even in children injury and subsequent inflammation of the vagina may produce occlusion, although stenosis, rare as a congenital condition, is more likely to result.

The existence of a rudimentary state of other portions of the genital apparatus, and the absence of tissue irregularities, cicatricial bands, and the remains of destructive inflammation, point to the congenital nature of the affection. Atresia of the hymen is very rare as an acquired condition.

The prognosis, in cases of vaginal atresia with retention, is almost without exception unfavorable, and this is especially the case when the fluid consists of menstrual blood. Where nothing is done, a fatal termination is invariably to be expected, through rupture of some part of the sac, or as a result of septic infection or peritonitis, independently of rupture. If perforation of the occluding membrane and evacuation of the cavity do occur, pyocolpos and pyometra follow with rare exceptions, and the danger to the patient, though less imminent, is hardly less certain. Even in spite of the most active treatment, the existence of a large sac secreting pus, which often is in free communication with the peritoneal cavity, is a constant source of apprehension, and a termination by no means favorable is to be anticipated.

In every case of atresia with retention it may be safely said that surgical intervention is urgently required. But even this is not free from danger or difficulty. For immediate rupture of a blood sac in the Fallopian tube may introduce a complication of the greatest gravity, or septic peritonitis may subsequently develop. In atresia hymenalis an operation is likely to be followed by a better result than in atresia vaginalis.

While the greater number of the congenital malformations of the female genitalia appeal only to the student of development and of pathological anatomy, vaginal atresias possess great clinical interest and are of the utmost practical importance. It is true that in a certain proportion of cases of vaginal atresia relief is sought before puberty is reached, and in other instances not until sexual intercourse proves to be difficult or impossible, and conception fails to occur; yet in the majority of cases of atresia, where suffering follows the establishment of the menstrual function and is dependent upon retention of the menstrual fluid, surgical intervention is urgently demanded. Almost without exception the condition of the patient is not recognized until this time, or else the obstruction could be divided before stasis had begun or before it had become considerable. The most satisfactory results are to be looked for when an operation is undertaken while there is yet no hæmatometra.

Although the methods of operating vary according to the nature of the obstruction and the taste of the operator, yet the indications are always the same. In every case an opening must be made through the occluding tissue (at a time midway between the two menstrual periods), sufficiently large to permit the free egress of the retained fluid, and this opening must be maintained in order that the sac may be thoroughly emptied and kept empty. In atresia without retention the same general plan of procedure is necessary, so that the vaginal tube may be kept sufficiently patulous to offer no obstacle to intercourse, conception, and delivery. Hymeneal atresias may be incised or punctured, and the opening thus made can be immediately or subsequently enlarged with the finger.

Atresias of the vagina which are simply due to an adhesion of its walls are sometimes easily broken down with the finger alone or with some blunt instrument. But if the atresia is due to a pronounced rudimentary condition of the genital canal, bloodless dilatation is hardly possible. In such cases the obstructing tissue must be carefully and slowly divided with a knife, or, preferably, with blunt-pointed scissors and the finger, a silver catheter guarding the urethra and bladder, and an assistant's finger the rectum, until the retention tumor is reached. Breisky, of Prague, who minutely describes the method of operating in high vaginal atresias, accompanied perhaps with atresia of the cervix, advises that as soon as the sac is encountered it should be punctured opposite the site of the cervix, or, if this cannot be found, at the lowest part of the vault of the tumor, with a long-handled lancet-shaped knife, the blade of which is surrounded and protected by a cannula. As soon as the blade has been projected from the cannula into the tumor, and the opening has been enlarged laterally, the knife is withdrawn and the cannula is pushed for some distance into the sac. The blades of a dilator, especially designed for this purpose, are next introduced alongside of the cannula, and the opening into the tumor can be enlarged in any direction, to any extent, or with any degree of rapidity that is deemed desirable. After this dilatation a German silver tube is introduced to serve for drainage, and likewise for the introduction of antiseptic fluids, and the dilator is removed. Whatever form of

drainage tube is employed, it should always be of some resistant material, and should be provided with large fenestrations. As the walls of the retention tumor subsequently contract, a tube smaller than the one first used should be substituted.

Although this mode of operating is based upon sound principles, and is intended to prevent any injury being done to the surrounding hollow organs and peritoneum, to enable the surgeon to control the rapidity of the escape of the retained fluid, and to maintain after the operation a free communication with the sac, yet it is quite probable that the same results could be achieved without the aid of the special instruments described, and with a greater degree of simplicity in manipulation.

The prognosis in cases of neglected vaginal atresia is unfavorable, nor is a more hopeful issue always to be anticipated after operation. Like many other gynecological procedures the danger here is out of proportion to the magnitude of the operation itself; for even puncture of a thin hymeneal septum may be followed by a fatal result.

The untoward accidents which may accompany or follow measures instituted for the relief of atresia vaginalis are: (1) injury of neighboring organs or of the peritoneum; (2) rupture of tubal blood sacs; and (3) septic infection.

The first of these dangers is not to be anticipated in operating upon the imperforate hymen or upon vaginal atresias of moderate extent, but where there is a considerable defect of the vaginal tube, and the atresia is broad and deeply seated, it requires the greatest care, especially when sharp-pointed instruments are used, to avoid wounding the urethra, bladder, rectum, or peritoneum.

Rupture of the tubes may follow operative interference in even the simplest forms of vaginal occlusion. The Fallopian tubes, distended with blood, or containing diverticula, or sacs filled with blood, are very prone, when the menstrual function has been established for some time, and there has been considerable retention, to form adhesions with surrounding tissues or organs. When the retained fluid is evacuated, and the distended genital canal collapses and contracts, great traction is exerted from below upon the fixed, thinned, and friable tubal wall, and rupture is very apt to occur. Increased pressure of the abdominal walls, blood forced by uterine contractions into the tube, and even contractions propagated from the uterine to the tubal wall, are said to increase the probability of this untoward accident. Rupture of the tube is a most unfortunate complication, to prevent which efforts have been made to alter slowly the size and position of the overfull uterus and vagina by withdrawing the fluid gradually through a small trocar puncture, or by several successive tappings. It is certainly wise to proceed slowly, and to withdraw the greater part, if not all, of the retained fluid through a small opening, which is to be enlarged after evacuation is completed. In this way changes in pressure occur slowly, and the genital canal has adequate time to adapt itself to its new position and surroundings. But the entire operation should be concluded at one sitting, or otherwise, while avoiding rupture of the tube, we court danger through septic infection, and subsequent disintegration of the tubal walls may occur as a result of this process. Breisky suggests that in some cases it might be well to perform abdominal section and remove the hæmatosalpinx, or incise and drain it, if such is known to exist, before the operation upon the atresia is attempted.

Septic infection, the third of the complications already mentioned, may be caused by absorption from the divided surfaces of the atresia, and the actual cautery and galvanic current have been used instead of the usual cutting and puncturing instruments in order to obviate this danger. But such an origin is somewhat questionable in view of the greater liability of the contents of an incompletely emptied sac to undergo decomposition, and the much greater importance which this factor assumes. It is septic decomposition and absorption which increase so signally the risk of repeated punctures and gradual evacuation. Emmet long ago showed the fallacy of this procedure, and the principles which he then urged upon the profession have now been accorded universal acceptance and approval. We should evacuate the cavity slowly if tubal rupture is anticipated, but, nevertheless, always at one sitting. Subsequent risk of decomposition within the sac is diminished by providing for adequate drainage. The sac immediately after operation may be thoroughly irrigated with an appropriate solution thrown into it under low pressure, and not so hot at first as to stimulate uterine contractions; but if the entrance of air is prevented, or only sterilized air is admitted, the danger to the patient is materially lessened. When the operation is performed with the spray and other antiseptic precautions, and the outer end of the drainage-tube is wrapped in some absorbent material impregnated with an efficient germicide, the outlook is rendered exceptionally favorable. Under certain circumstances it might be judicious to postpone washing out the canal until after evidences of decomposition have become apparent, in the meanwhile care being exercised to secure adequate drainage. Irrigation is always indicated when pyocolpos and pyometra are recognized.

When the immediate danger to the patient is over, the physician is confronted with the problem of how best to keep patulous the opening that has been made. The tendency of artificial passages through extensive atresias to close is remarkable; various plans have been suggested to obviate this difficulty. The use of the glass tube, which can be introduced into the vagina by the patient, and can be worn for as long a time as is desirable, is especially commended by Emmet. Breisky, on the contrary, prefers dilatation with the fingers or speculum, to be begun eight days after the operation, and to be repeated at suitable intervals. If the divided edges can be covered with a flap of skin or mucous membrane, as has been done in exceptional instances, an excellent result is assured. Cohabitation, if the patient be married, materially assists subsequent efforts to keep the canal open. Puncture of hæmatocolpos through the rectum or bladder should be mentioned only to be condemned.

C. *Congenital Stenosis of the Simple Vagina.*—While atresia of the vagina means complete, stenosis implies only partial, occlusion of that canal, so that menstrual blood can find an exit, and conception can take place, things impossible in the former and more rare condition.

As in atresia, the hymen or the vaginal canal above it may be affected, though congenital stenosis of the hymen is uncommon. There may be a septum perforated with openings so small as only to become apparent when the menstrual blood trickles through them, or bands of tissue extending from one portion of the vagina to another, or again, spiral or ring-shaped folds projecting from the vaginal surface. Pronounced stenoses are not commonly encountered where the remaining portions of the genital apparatus are normally developed.

The same causes which produce atresia of the vagina, though operating less actively, occasion stenosis of this canal, namely, fœtal inflammatory processes occurring late in embryonal development, and overgrowth of the hymeneal folds.

In this condition there may perhaps be temporary amenorrhœa when the stenosis is very pronounced, followed by dysmenorrhœa from forcible contractions of the vagina and uterus; but since there is always some opening for the escape of menstrual blood there is no development of a retention tumor nor of the painful and alarming disturbances incident thereto. Cohabitation may be interfered with, but there is no insuperable obstacle to conception, and while labor is occasionally made tedious and difficult, the characteristic tissue changes of pregnancy often render the structures soft and dilatable. Still, in certain cases, without surgical intervention delivery cannot be accomplished, and even rupture of the vagina during labor has been known to occur.

The diagnosis is easy, as a rule, although it may sometimes be difficult to find an opening, and the condition is

hence mistaken for an atresia. It is, however, not impossible to confound acquired with congenital stenosis, and a spasm of the muscles of the pelvic floor may lead one into error.

For obvious reasons the prognosis in stenosis presents none of the grave aspects that characterize atresia of the vagina.

When to lessen the difficulties attending coition, and to increase the probabilities of conception, it is desirable to enlarge the strictured vaginal canal, this may be accomplished by the use of tents, sounds, dilators, and the like, but the results are never so satisfactory as when the edges of the occluding bands or folds are incised, and dilatation by speculum or antiseptic tamponing is afterward systematically employed. Cohabitation alone often ultimately achieves the desired end, and during labor the advancing head accomplishes an extraordinary degree of dilatation. Yet it is never safe at this crisis to rely entirely upon nature's efforts to overcome the obstruction, for the most untoward accidents have been known to occur. It is best during delivery to divide at once any obstructing band which seems likely to delay materially the progress of the child, though incision should always be made as superficially as possible.

D. *Divided or Duplex Vagina.*—In this condition the vagina is divided into two lateral halves, rarely of equal dimensions, by a more or less perfect septum, consisting of two folds of mucous membrane, separated by a little muscular and connective tissue. This partition may be complete, or may be perforated by a number of openings, or its presence may alone be indicated by a band or by bands of tissue connecting the upper, middle, or lower portions of the anterior and posterior vaginal walls. With double vagina the uterus is usually also double, but may be single, and there may be a portion in each half of the vagina, or the uterus may have two openings in one side and none in the other. When the uterus is single and the vagina double, only that half of the latter is suitable for coition which ends in a cul-de-sac above; and in one-horned uterus, with atrophied second horn, the side of the vagina which corresponds to the atrophied half of the uterus is generally found in a very rudimentary condition.

There may be atresia of both halves of a duplex vagina, although one side—in a vast majority of cases the right—is alone occluded as a rule. As a result of this, bilateral or unilateral hæmatocolpos may develop. Spontaneous perforation of the obstructing membrane and evacuation of the contained fluid, and rupture of tubal blood sacs, occur more often here than in the case of atresia of the simple vagina.

Duplexity of the vagina results from a persistence of the septum between the Müllerian ducts, which should have completely disappeared by the end of the twelfth week of embryonal life. Coalescence of the two ducts of Müller begins not far from their points of outlet, between the lower and middle thirds of the future genital tract, and extends upward and downward, but more slowly in the former than in the latter direction. A single vagina with a double uterus is hence a more common condition than a double vagina with a single womb.

The septum of a duplex vagina may interfere with coitus, and during labor the descending fœtal extremity may not follow either canal, displacing the partition laterally, but may push the septum or band before it, delivery being thus impeded.

When there is atresia of both halves of a duplex vagina the symptoms will be almost identical with those accompanying occlusion of the simple canal. When, however, only one half is obstructed, moliminal disturbances will occur with retention in the obstructed half (hæmatocolpos and hæmatometra lateralis), but a menstrual discharge will regularly escape from the patent portion of the tube, and in the intermenstrual periods a catarrhal outflow will occur.

The diagnosis is facilitated by remembering that in this condition there are present all the symptoms accompanying atresia of the simple vagina with the exception of amenorrhœa; the menstrual flow regularly recurs and the retention tumor that is developed has a distinctly lateral situation. This latter fact may lead the examiner to confuse hæmatometra and hæmatocolpos lateralis with peri-uterine hæmatocele, with cystic enlargements of the ovary and Fallopian tube, or with soft uterine myomata. But if the atresia is seated near the vaginal outlet, no such error is likely to arise, and familiarity with the history of the case will usually solve any apparent difficulties.

The same dangers attend atresias of the double vagina that are present in obstruction of the simple canal. Rupture of the Fallopian tubes may occur, or, after spontaneous perforation of the occluding diaphragm, pyocolpos and pyometra may develop with subsequent involvement of the tubes and pelvic peritoneum, or the patient's general health may suffer seriously from the long-continued suppuration and purulent discharge.

The septum can be divided with scissors without much risk of hemorrhage even during labor, when it offers, or seems likely to offer, any serious obstacle to delivery, or in the non-pregnant female when intercourse is difficult or conception impossible.

E. *Faulty Communications with Other Cavities.*—If it be remembered that in the embryo the urogenital tube and the intestinal tube terminate in a common conduit—the cloaca, a depression on the external surface of the ovum,—the genesis of the abnormalities in question is easily explicable. In the normal course of development a septum (completed in the tenth week of intra-uterine existence) divides the urogenital sinus in front from the rectum behind. If this septum does not appear the cloaca persists, there is no anus, and apparently the rectum empties into the vagina a short distance above the hymen. To this condition the strange name atresia ani vaginalis has been accorded; while if the communication is below the hymen, it is called atresia ani hymenalis or vestibularis. The simple term persistent cloaca would more accurately describe both abnormalities. The opening of the intestinal canal into the cloaca may be small, and, if not actually possessing a sphincter, may yet be able to resist the involuntary passage of fæces and flatus; which are voided periodically and at will. If the communication be large, however, the patient suffers from those symptoms which characterize the more extensive forms of perineal laceration.

Numerous other abnormal communications have been observed, as, for example, an opening from the vagina into the normally formed rectum, from the vagina into the urethra or bladder, or between a ureter and the vagina. Again, the ileum, colon, and vagina have been found opening upon the surface of an extroverted bladder.

The sinus urogenitalis may persist as a long and narrow passage, so that the urethra opens, apparently, not into the vestibule, but into the vagina.

The causes of these faulty communications are largely arrests in development occasioned by fœtal inflammatory processes; but in the production of persistent cloaca (atresia ani vaginalis or vestibularis) hereditary influence seems to have some force, since this condition has been known to have been present in several members of the same family.

For the relief of this last condition the perineum should be divided from before backward, the end of the intestine is to be sutured in the middle of the incision thus made, and the remainder of the wound closed by stitches. The abnormal opening into the vagina will often close spontaneously.

F. *Blind Canals or Inversions of Vaginal Mucous Membrane.*—Occasionally lacunæ of the vagina attain unusual dimensions and are recognized as blind tubes, sometimes large and long enough to admit the little finger, lined with smooth mucous membrane and lying parallel to the long axis of the vagina, or they are deflected into the perivaginal connective tissue. The point of exit of these tubes is usually near the vaginal outlet at the sides of the columna ruga posterior.

G. *Infantile Vagina.*—Sometimes the vagina, though perfectly developed, from an arrest of growth in childhood, fails to attain adequate dimensions, and retains its infantile character throughout later life, being too short, too narrow, or both. Uterus fœtalis and uterus infantilis are not infrequently associated with this condition.

George Woodruff Johnston.

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VAGINA, DISEASES OF.—I. CYSTS.—Cysts of the vagina are not met with very frequently. Usually they are located in the lower third of the vagina and occur with equal frequency upon either the anterior or the posterior wall. When deep-seated they are small and do not encroach much upon the lumen of the vagina, but as they increase in size the vaginal mucous membrane becomes distended, loses its characteristic wrinkles and assumes the appearance of an ovarian tumor, especially when it protrudes at the vulva. As a rule they grow slowly and rarely attain a great size. These cysts may be of glandular origin or may have their origin in the remains of the Wolffian bodies. In those cases in which several cysts are found connected in a row at the side of the vagina they have doubtless originated in local dilatations either of one of Gärtner's ducts or of an undeveloped duct of Müller. The contents of the cysts are usually a clear yellowish transparent fluid, but they may be discolored by disorganized blood which has escaped into them. They rarely give any symptoms beyond that of mechanical obstruction. It is well to remember, in making a diagnosis, that these cysts have been mistaken for cystocele, rectocele, urethrocele, vaginal hernia, and cysts of the vulvovaginal gland. In all cases of vaginal cyst it is best to remove them except in old women in whom the tumor is small. They may be punctured and drained, or injected with some irritating fluid to set up an obliterating inflammation, or they may be dissected out. The last sometimes proves a most tedious and difficult procedure. Schroeder's operation consists in removing by scissors all of the cyst wall that rises above the level of the vagina and

FIG. 4941.—Diagrammatic Representation of Combined Cystocele and Urethrocele. (From Mundé's "Gynæcology.")

stitching the mucous membrane of the vagina about the circumference of the excavation to the cyst wall. The surface occupied by the remainder of the cyst soon assumes the character of the vaginal mucous membrane, the cavity becomes flattened out, and no trace of the tumor remains. In this connection it may be well to mention the fact that large blebs are sometimes found in the va-

FIG. 4942.—Diagram showing Hypertrophy of the Tissues below the Urethra. (From Mundé's "Gynæcology.")

gina, and have been named by some authorities air cysts of the vagina. They are usually found in the upper portion of the canal. They collapse on puncture or they rupture and disappear. They are more apt to be present during gestation than at any other period.

II. NEW GROWTHS.—Carcinoma has been known to develop primarily in the vagina, but as a rule the only malignant growths observed in the vagina are those which have developed primarily in the uterus. For information in regard to them the reader is referred to the article entitled *Uterus, Diseases of: Malignant New Growths.*

III. VESICO-VAGINAL CYSTOCELE.—Cystocele is a descent or prolapse of the base of the bladder into the vagina, and declares itself by the presence of a protruding mass at the introitus vaginæ. It varies in size from a small ovoid to a large mass protruding entirely out of the vulva (Fig. 4941). Under the latter circumstances it is usually accompanied by procidentia of the uterus and prolapse of the rectum. A cystocele partakes of the character of a true hernia, and in its ordinary form must be regarded as a hernia of the bladder which protrudes into the vaginal canal and presents itself at the vulva. The symptoms which are steadily progressive are dysuria, retention, and incontinence due to overdistention. Later, there may follow cystitis, ureteritis, pyelitis, rarely a vesical calculus. The etiology of the condition varies in different periods of life. In virgins and nulliparæ it is due to a supravaginal elongation of the cervix, occasioned primarily by hypertrophy of the uterine tissue. This permits the descent of the upper supports of the vagina, producing a sagging of its anterior wall and the base of the bladder. This initial elongation pushes down the vaginal supports; but later the rôles are reversed and the vaginal prolapse drags down and increases the elongation of the cervix. In multiparæ the condition is usually associated with laceration of the cervix and perineum, with retrodisplacement and descent of the uterus. In the process of parturition the anterior vaginal wall, as well as the other parts, has suffered serious injury, reducing its resisting power and permitting the development of the hernial pouch into which the bladder descends. The diagnosis of the condition is not difficult. A protruding mass presents itself at the vulva; it is soft and flabby when the bladder is empty, tense and elastic

when the bladder is full. A sound passed through the urethra readily turns down into the protruding tumor, and by means of this the boundaries of the bladder may be readily determined.

The condition of urethrocele must be distinguished from that of hypertrophy of the tissues which lie below the urethra. This latter condition is by no means uncommon (see Fig. 4942).

Treatment.—In aged women in whom an operative procedure is not advisable on account of the dangers of anæsthesia, shock, and depression, a pessary can usually be fitted to retain the mass in the vagina and thus afford relief. The Gehrung hard-rubber pessary has been found most serviceable for this purpose. A soft-rubber ball that can be inflated after insertion is effective, but requires constant attention and frequent renewals. Such devices are merely temporary expedients. For permanent relief some operative procedure must be resorted to. Sims and Emmet were very ingenious in devising different methods of plastic work upon the vaginal wall, and they carried these methods to a high degree of perfection.

The fundamental idea in these methods was to denude areas of various sizes and shapes in the mucous membrane of the vagina, and then to cover them over by introducing sutures into the surrounding edges of the mucous membrane and drawing upon them until all the slack over the hernial mass had been taken in. These operations took the name of *colporrhaphy*. The stitches were usually passed in a transverse direction. Stoltz simplified this by merely denuding an oval or round area of mucous membrane, the size varying with the size of the cystocele, and then drawing the edges together with a puckering string, which had been passed around the circumference of the denuded area, about one-third of an inch from the edge. This string was worked in and out of the mucous membrane, like the gathering string of a tobacco pouch. All of these operations, however, failed to give permanent relief. Sooner or later the steady pressure caused the contracted tissue to stretch and eventually to give way, and thus the original condition was reproduced. The true cause of the difficulty was not overcome by these methods.

If it be granted that a cystocele is a hernia, it would seem quite as rational a procedure, and would give promise of quite as satisfactory results, to denude the skin over an inguinal hernia and bring the edges together with stitches, as to expect to cure a cystocele by simply denuding the vaginal mucous membrane and covering in the raw surface. The fascia is the sustaining tissue in all herniæ, and the only permanent relief consists in cutting out the overdistended and atrophied area of fascia and bringing into apposition the edges of the strong, well-nourished areas that have either resisted, or have not been subjected to, the destructive pressure. In the relief of cystocele, however, the bladder does not adapt itself to the new condition so readily as the intestines do after an operation for inguinal hernia. The base of the bladder, by reason of the diminution in the extent of the vaginal wall, is thrown into wrinkles and folds, producing pockets in which the urine may accumulate, be retained, undergo decomposition, and inaugurate the unfortunate sequelæ of cystitis, calculus, ureteritis, pyelitis, etc. Some way must be provided, therefore, for smoothing out the redundant tissue of the bladder wall produced by the operation upon the fascia. This is all accomplished in the author's procedure, as follows:

The Author's Operation for Cystocele.—This device has for its object the attainment of two distinct results: First, to free the wall of the bladder from all connection with the vagina, as the contents of an inguinal hernia are freed from the sac, so that all of the overstretched vaginal sheath or fascia, and vaginal mucous membrane as well, may be cut away and the well-nourished areas secured for support of the bladder; and, second, to smooth out the redundant base of the bladder produced

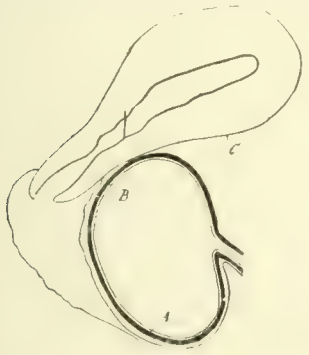

Fig. 4943.

Fig. 4944.

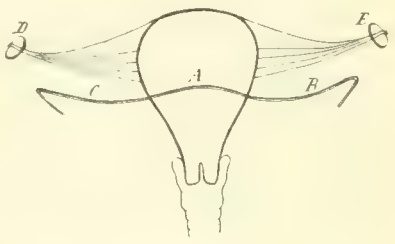

Fig. 4945.

Figs. 4943, 4944, and 4945. Diagram showing some of the Details of the Author's Operation for the Relief of a Vesico-Vaginal Cystocele, and the Principle upon which it is Based. Fig. 4943 shows the position of the bladder and its relations to the uterus before the operation. After the bladder has been freed from its sheath, it is rotated on its transverse diameter until the point *A* is carried up to *B*, and the point *B* to *C*. The effect of this is shown in Fig. 4944. The bladder is then stitched in its new position, in which its base (from *A* to the urethra) forms a straight line. In Fig. 4945 the line *A B C* corresponds with that of the tear through the peritoneum across the face of the uterus and broad ligaments, *C* and *B* being the points at which the corners of the bladder are attached on either side; *D* and *E* represent the internal abdominal rings through which the round ligaments pass.

By thus diminishing the size of its capsule. The technique of the operation is as follows: A transverse incision is made through the vaginal wall just in front of the cervix, as for vaginal hysterectomy. Through this the bladder is dissected from the uterus and the peritoneal cavity entered, the peritoneum being torn well out to either side. A longitudinal incision is then made in the anterior vaginal wall from the middle point of the transverse incision to the neck of the bladder. Through this the bladder wall is freely dissected from the vaginal wall on either side until its base is set entirely free. The bladder is now rotated upon its transverse axis, the base being carried up against the face of the uterus and stitched there with chromicized catgut. In doing this the surgeon should select, in the base of the bladder, a point so situated that by stitching this particular part of the bladder to the uterus he will cause all the slack between the latter organ and the symphysis pubis to disappear. He should next select, on the sides of the bladder, two other points equally distant from the median line and on the same level with the points first selected, and by means of sutures he should firmly attach these two parts of the bladder-wall to the torn edges of the peritoneum on the face of the broad ligaments. In doing this, however, he should be careful to insert the sutures into each broad ligament at points far enough removed from the median line to cause them, when tied, to take in all the slack in the base of the bladder from side to side. The effect of this mode of employing sutures is to

stretch the bladder taut and smooth in every direction. The fascia and mucous membrane along the longitudinal line of the vaginal incision are now trimmed off sufficiently to make them fit snugly the base of the bladder, and they are then to be stitched together with interrupted sutures of chromicized gut. The dressing consists of a light packing of gauze in the vagina. In cases in which lacerations of the cervix and perineum complicate the cystocele, these injuries should be repaired at the same sitting. If displacement of the uterus also exists, this may be relieved by shortening the round ligaments through the anterior vaginal incision previous to stitching up the bladder.

IV. Diseases of the Vulva.—The vulva, the pudenda, or the external genitals of the female, comprise all the structures immediately external to the hymen and surrounding the entrance to the vagina. Anatomically these parts are very distinct. Posterior to the hymen are the fossa navicularis, the posterior commissure or fourchette, and the perineum. Anteriorly are the urethral orifice, the vestibule, the clitoris, and the mons veneris, and at the sides the labia minora (sometimes called the nymphæ because they preside over the water brooks), and the labia majora. It is important to recognize the position of certain ducts opening in the mucous membrane of these parts. The most important of these are: the Bartholinian ducts, which supply an exit for the secretions of the glands of the same name, and whose orifices lie at either side of the hymen and exterior to it; and the mucous crypts known as Skene's glands, which may be found inside the meatus urinarius. These ducts, as well as the meatus, are the frequent foci of inflammation in the mucous membrane of the vulva. The hymen marks the boundary between the external and internal organs of generation, and may be classified as belonging either to the vulva or to the vagina. When intact, or in its caruncular form after rupture, it participates in all inflammatory processes of the vagina or vulva.

The function of the vulva is to close the entrance to the vagina and to protect it against the entrance of air, dust, and bacteria. This is accomplished not only by the contact of the labia due to their anatomical position, but by the adhesive secretions which cover their internal surfaces and agglutinate them together. The importance of this function has become clearer during recent years, as we have realized that air and dust are the carriers of bacteria, and that bacteria are the source of inflammation.

The *hygiene of the vulva* is a subject that has been sadly disregarded, and yet is of supreme importance in preserving the health of the genital organs of girls and of women. In the proper observance of the laws of hygiene applicable to these parts lies the prophylaxis of many of the inflammations of the genital tract. Only the commonest attention to cleanliness is necessary to prevent the accumulation of secretions in the creases and folds of the pudenda, and yet it is a very common experience in examining women, even of the better class, and those who would be insulted if they were told that they were not cleanly, to find accumulations of smegma, in the sulci between the labia minora and majora and about the clitoris, discolored with dirt and of most unpleasant odor. Muco-purulent discharges also frequently escape between the labia and smear their external surfaces. Such secretions afford a lodging-place for the clouds of dust that roll up from the street under the women's skirts, and become culture media for all sorts of micro-organisms, which travel from these foci along the genital tract to the vagina, cervix uteri, fundus, and Fallopian tubes. The proximity of the anus is another source of bacterial infection, and therefore in women especially it demands hygienic care. These parts certainly demand as frequent bathing as the face, and should be thoroughly cleansed with soap and water at least once every day. Open drawers, so commonly worn by women, expose these parts to contact of street dust. They should never be worn The tight drawers afford the only efficient protection against street dust and sudden changes of temperature, in both old and young. Women should also be taught to change the napkin frequently during the monthly molimen, whether it becomes saturated or not. Menstrual discharges take on fermentation very promptly, and when kept for several hours in contact with the heated parts about the vulva, they not only make the individual offensive, but become active sources of infection to the genital tract. If the menstrual flux is free or excessive, the necessity for frequent changes of napkin can be obviated by taking a tepid aseptic vaginal douche for cleansing purposes once or twice each day. By having the temperature of the fluid used in the douche at 110°–115° F., the amount of the flow can be materially lessened or entirely interrupted. When the douche is used simply for cleansing purposes, the temperature of the water should not be above 100° F.

Through tradition as well as in accordance with the Hebrew law it has long been accepted as axiomatic that a woman should not bathe during the monthly molimen. A moment's reflection should satisfy any reasonable person that such teaching is unwise. If there is ever a time in a woman's life when she needs a tub bath it is during the days of menstruation. During this period not only are the glands of the genital tract stimulated to an unwonted degree, but the cutaneous glands of the groins and axillæ, and indeed of the entire surface of the body, take on unusual activity. These sudoriferous and sebaceous excretions, if not removed by the daily bath, undergo fermentative changes, become rancid and foul-smelling, rendering many an otherwise attractive creature anything but an agreeable companion. Women are aware of this, and, to overcome it and make their presence less offensive, they saturate their handkerchiefs and clothing with perfumery of all kinds. In the mean time the pores of the skin become occluded with accumulations of excretions, the glands cease to do their physiological work, and the woman suffers from headache and indigestion.

Malformation of the Vulva.—The key to all malformations is usually to be found in the embryology of the affected part. The malformation is the result either of a lack of development, an excessive development, or a misdirected development. In the vulva the first and simplest form, although not the most common, is illustrated by what is known as the infantile vulva, *i.e.*, the character of the vulva during infancy persists into adult life. The labia majora are less developed than the other parts, the vulvar cleft being more exposed to view. The mons veneris is lacking in prominence, and there is absence of hair. The persistence of this form of the vulva is usually indicative of imperfect development of the internal generative organs as well. The type of excessive development is seen in cases of double vulva. Three such cases have been observed and recorded. In these there were two vulvæ situated side by side in the interfemoral space. The type is exhibited in what is known as pseudohermaphroditism, in which there is such an excess of development of some parts and lack of development of others, or such a confusion of development of the apparent organs of both sexes that it becomes difficult to decide to which sex the individual belongs. Such cases are rare, and are interesting as curiosities or freaks of nature rather than as cases for medical or surgical treatment.

A condition of practical importance is that of *vulvar atresia*. This is produced by more or less permanent adhesions between the labia of opposite sides, thus apparently obliterating the vulvar cleft. There is usually a small opening anteriorly, through which the urine finds exit with greater or less difficulty, but the menstrual discharge is frequently retained in these cases. But even if the discharge be not retained, trouble is apt to arise when attempts at sexual intercourse are made. The labial adhesions may give way under this pressure, or it may be necessary to dissect them apart. Sometimes the labia may be torn apart, but if this occurs in the nuptial bed serious hemorrhage may result. Adhesions may not be confined simply to the labia; they may also involve the clitoris and the prepuce, or adhesions between these parts may exist independently. This condition is analogous anatomically to the adherent prepuce in the male,

and may be attended with similar nervous symptoms, even persisting to adult life. The treatment consists in freeing the tissues from these adhesions. This may be accomplished in some cases by simple manipulation with the fingers. In other cases, however, the adhesions have become so thoroughly organized as to require careful dissection under general anæsthesia.

Vulvo-vaginal Anus.—This malformation, known under various names as anus vulvalis, vulvar anus, atresia ani vaginalis, or atresia ani vestibularis, is the result of arrested development at the cloacal stage. There is no anal opening in the normal position, the contents of the rectum finding exit through an opening near the site of the hymen, either external or internal to it. There may be two openings near to each other, or one may be at the normal site of the anus and the other at the hymen. In some of these cases the patient may have satisfactory control of the movements of the bowels. Under such circumstances the discovery of the condition may be entirely accidental, and no surgical interference is required. But when fæcal incontinence exists, operative measures become necessary. The effort of the surgeon should be to make an artificial anus at the normal seat of that orifice. Control may be secured by splitting the fibres of the levator ani muscle and dragging the rectum through to secure sphincteric control, or the rectum may be twisted upon itself 180° for the purpose of securing a valve-like action, or both devices may be employed. To relieve this condition effectually requires all the ingenuity of the most experienced plastic surgeon. Some authorities advise delaying all interference till the age of puberty. But there are many reasons for the opinion that the earlier the abnormality is relieved the better. In the young and formative years nature will do more toward developing sphincteric control than in later years. Moreover, by early repair the child will be saved years of discomfort and embarrassment that would necessarily retard its mental, moral, and physical development.

Analogous to the condition just described are the malformations known as *hypospadias* and *epispadias*. In the former the posterior wall of the urethra is lacking, and in the latter the anterior wall. Epispadias may be accompanied by extroversion of the bladder or by extension of the sinus to the clitoris, dividing it into two parts. The one symptom of these conditions is incontinence of urine. Control may be secured by plastic operations, and in cases in which sufficient length of urethra can be secured for the purpose, the urethra may be dissected out and twisted on its longitudinal axis one-fourth or one-half the circumference of a circle and stitched in that position.

Injuries of the Vulva.—These may be due to external violence, to coitus, or to parturition, and are serious on account of the profuse hemorrhage that is apt to attend them. The patient may fall astride a stepladder or the back of a chair, or as a child she may fall on a picket fence, or in sliding down an incline may transfix these parts on any pointed object. There is on record the case of a child who, on sliding down from a haymow, came astride the sharp stake of a hayrack. The stake entered at the vulva, passed up through the abdomen, and made its exit below the ninth rib of the left side, entirely transfixing the body. It is noteworthy that the child recovered and lived for three years, dying finally of scarlet fever.

Bicyclists may be thrown from their saddles upon the frames or handle-bars of their wheels and receive serious injuries of the vulva. Coitus rarely produces injuries except in cases of rape in children and women of advanced years. In such cases damage is done to the hymen, the fourchette, and the posterior wall of the vagina. In parturition the vulva may suffer from contusions or lacerations by the head of the child or from the unskilful use of the forceps. In cases of external violence and in puerperal cases it is well to remember that there may be deep hemorrhage into the connective tissue, resulting in hæmatocele. The tumor thus formed may be small and inconspicuous, or it may assume large proportions, dissecting into the connective tissue of the pudenda, and even spreading up into the abdominal wall. The tension upon the external tissue may be so great as to cause rupture of the walls of the tumor and allow the clots to escape. If an artery is involved in the injury, the condition may be converted into one of actual hemorrhage. In a small hæmatocele the clot under gentle pressure usually becomes absorbed, but in cases of severe contusion or of excessive hemorrhage gangrene may supervene. The symptoms of pudendal hæmatoma or hæmatocele are rapid swelling of the labia and pain. Discoloration of the skin follows, the color changing from red to blue and green, and, as absorption progresses, to bronze. The tumor at first is tense, but gradually it becomes boggy and soft. If the hemorrhage is copious, there may be symptoms of shock. The treatment consists in stopping the hemorrhage, if still in its active stage, by applications of ice, or by pressure effected by means of pads and bandages. If this is not effectual and the tumor continues to develop rapidly, it may be necessary to cut down upon the bleeding vessels and secure them by ligature. If in due time absorption does not set in, and the tumor shows signs of breaking down and suppurating, with more or less elevation of temperature, the tumor must be treated as an abscess, *i.e.*, by free incision and drainage.

Vulvitis.—If we accept the modern scientific dictum that all inflammation is the manifestation, or the result, of an invasion by micro-organisms, inflammations of the vulva may be classified according to the genus of the infecting organism. But, as all the infecting germs have not yet been discovered, and as the part played by each organism in a mixed infection has not been positively determined, the clinical picture, the signs, and symptoms must still be depended upon in many instances as a reliable guide to diagnosis and treatment. Irritating discharges from the vagina, which spring from gonorrhœal or from septic inflammation of the vagina or the uterus or from cancerous ulceration of the cervix, may cause inflammation of the vulva. The infection may come from without or from the morbid germs carried in the discharges. In such cases applications of silver nitrate in solution (1 in 20), should be made to the external parts after they have been thoroughly cleansed, and then some protecting ointment, as oxide of zinc, should be applied. At the same time vigorous treatment must be directed to the cause of the disease.

Aphthæ or thrush of the vulva is an infection similar to that which invades infants' and children's mouths. It is apt to attack nursing women. The infecting agent is the vegetative organism oïdium albicans. The disease is characterized by a white exudate elevated on an inflammatory base. It occurs in discrete patches. The treatment consists in bathing the parts thoroughly with a solution of bichloride of mercury (1 in 2,000),—the procedure to be repeated daily.

Chancre and chancroid of the vulva have the same significance and characteristics as the same lesions in other parts, and the treatment is the same.

Diphtheria of the vulva is found almost exclusively in puerperal women, although it may attack children. It is usually ushered in by a severe chill, followed by a sharp rise of temperature to 104° or 105° F., and a rapid and feeble pulse. Inspection reveals the presence of the yellowish-gray membrane containing the Klebs-Loeffler bacillus. Thorough antiseptic washes should be employed and prompt constitutional treatment instituted. Full doses of antitoxin hypodermatically are the sheet anchor.

Erysipelas of the vulva is due to the invasion of the streptococcus erysipelatis, and is recognized as a desperate condition. It may follow operations upon the external genitals, may appear without warning as a complication of diabetes mellitus, especially in aged women, or may be the first stage in the march of invasion of a puerperal sepsis. In the last instance the serious symptoms manifest themselves in the uterus and adjoining structures. The rich supply of lymph spaces and channels in and about the pudendal structures afford a good field for the spread of this particular infection, and the

treatment should be prompt and vigorous, both sustaining and local. Iron internally and lead and opium wash externally still hold as the specifics. The bowels should be kept freely open with salines.

Skin Diseases of the Vulva.—Skin diseases have been treated very fully in the articles devoted to them, but there are certain localized conditions of the skin of the external genitals which come more directly under the care of the gynecologist, and which may therefore properly be considered here. Among these may be mentioned such common affections as intertrigo, erythema, and eczema, all of which are largely the result of filth. Thorough and persistent attention to cleanliness, and, in aggravated cases, the employment of soothing lotions or dusting powders, constitute all the treatment that is called for.

Folliculitis is a pustular eruption due to the invasion of the hair follicles by the staphylococcus pyogenes albus, aureus, or citreus. The entire skin surface of the vulva may be completely covered with conical-shaped pustules, each having a hair springing from its summit. The disease is apt to occur in anæmic, debilitated women, but is due directly to lack of cleanliness. Sometimes the skin is red and inflamed, and burning and itching may be present. In other cases there will be no unusual sensation whatsoever, the pustules being discovered by accident, as it were, after they have invaded a large area of tissue. Constitutionally the treatment should be sustaining, and locally the application of strong antiseptics is indicated. Moist dressings of bichloride of mercury, 1 in 2,000, or carbolized or sulphurated ointments, may be applied to the affected skin, for the purpose of promptly destroying the infecting agent. Epilation is usually unnecessary.

Herpes genitalis has already been discussed in sufficient detail in a previous volume (Vol. IV., page 685).

The parasitic affections of the vulva, *i.e.*, the common ones, are eczema marginatum, or ringworm, and the irritation caused by the pediculus pubis. The former appears in reddish, moist, pigmented areas, of circular or curved form, and with raised borders. Over the surface of these areas are scattered small vesicles or pustules with yellowish crusts. These may be confined to the labia or they may spread back to the anus or forward over the mons veneris and abdomen, and out on to the thighs. The sovereign remedy is sulphur, either in the form of sulphurous acid on compresses, or as one of the sulphur ointments. The pediculus or louse that infests the hairy parts of the pubes is a crab-like insect, and can be found holding fast to a hair, and inserting its proboscis into the sebaceous follicle, from which it derives its sustenance. It produces an intense itching. When the presence of the parasite, however, is once discovered, relief is promptly secured by one or two applications of mercurial ointment (blue ointment), which destroys both the insect and the nits.

Pruritus Vulvæ.—Many affections of the vulva are attended with the most intense burning and itching. In neurotic patients it becomes absolutely intolerable, and in some instances causes loss of sleep, physical exhaustion, and nervous depression leading to melancholia and other forms of insanity. The distress may be aggravated by the effort to procure relief by scratching or rubbing the parts. In this way sexual excitement and orgasm are produced and a habit of masturbation is established.

Pruritus is only a symptom, but like dysmenorrhœa it is so common and persistent, and withal so obscure in its etiology, that it demands a special chapter for itself in all gynecologic treatises, even the most recent and scientific. It will be treated here under the following headings: Puerperal pruritus, diabetic pruritus, parasitic pruritus, and neurotic pruritus—also termed kraurosis vulvæ.

Puerperal Pruritus.—Pruritus is not an unusual accompaniment of pregnancy, and may arise at any time during the period of gestation. At this time the secretions from the glands about the vulva and vagina are markedly increased, and, unless the patient is scrupulously clean, they are apt to become culture media for irritating microorganisms.

In this variety of pruritus, as in all cases of this affection, the parts should be carefully inspected to exclude parasites, the urine should be examined to exclude or confirm the presence of diabetes mellitus, and the amount of the local secretions should be determined.

If parasites or diabetes be present, the appropriate treatment should be applied; otherwise hygienic measures should be prescribed, including sitz-baths and vaginal douches of bichloride of mercury or carbolic-acid solutions. Local applications of black wash (oxide of mercury), carbolic-acid solution (1 in 40), or Unguentum zinci oxidi are also efficient.

Pruritus is one of the early symptoms of diabetes mellitus, and in all cases of itching and burning of the vulva the urine should be examined for the presence of sugar. The exhibition of appropriate treatment for this disease will permanently relieve the local symptoms. Local applications, similar to those recommended above, may be necessary for immediate relief.

The two parasites that most commonly infest these regions are the pediculus pubis and the trichophyton tonsurans or ringworm. The former seeks its habitat among the hairs of the pubes, gaining its sustenance from the sebaceous glands about the hair follicles. It hangs with its head seemingly buried in the skin, and is difficult to remove. This insect is commonly known as the crab louse. It deposits its eggs or nits on the hair shafts. Two or three applications of Unguentum hydrargyri (blue ointment) will destroy both the insect and the nits. Kerosene oil also acts efficiently.

Kraurosis vulvæ is characterized by a withered, parchment-like appearance of the surfaces of the labia majora and the external surfaces of the nymphæ. It may also extend to the mons veneris and the tissues about the clitoris. The folds are gradually obliterated, and there is a general contraction of the introitus vaginæ. Intercourse is extremely painful, and an intolerable burning and itching persist during the early stages. These latter symptoms may become intermittent as the disease progresses. In the early stages there may be thickened, hypertrophied areas of skin which are sensitive to the touch; they are interspersed throughout the areas of sclerosed atrophic tissue. Gradually the whole surface becomes atrophic and takes on the parchment-like appearance. The disease, which comes late in life, usually after the menopause, is a progressive one, and is relieved only by the removal, by dissection, of all the vulva. It is not necessary to postpone the operation until the disease has become self-limited. The amount of tissue removed is of no great importance except that it should include all that may possibly be invaded. The operation consists in making an incision, at the junction of the skin and mucous membrane, from the clitoris around the entire circumference of the introitus. A second incision, concentric with the first, is made through the skin around the entire vulva at the outer margin of the invaded tissue. The tissue included between these two incisions is next dissected out. The edges are then coaptated by interrupted sutures of chromicized catgut or silkworm gut. Bleeding parts may be secured by ligature, but the general oozing is controlled by the sutures. In cases in which the disease invades the mons it is necessary to include the clitoris in the exsected tissue. A strong ligature of catgut, transfixing the clitoris at its base, will control hemorrhage from the vessels of that organ. In applying the stitches the parts should be adjusted, as the necessities of the case require, to give nice apposition.

Hypertrophy of the Vulva.—Hypertrophy of the clitoris is not uncommon. It may be congenital or acquired. It usually accompanies those malformations which go to make the pseudohermaphrodite. Fehling has reported the case of a girl, twenty-one years of age, with a clitoris five inches long, an inch and one-half thick, terminating in a glans one inch long. Hypertrophy of the labia minora, especially elongation, is not infrequently met in gynecologic practice. Certain pathologic processes may

produce this; it may also be congenital or it may be the result of manipulation. As is well known, the Hottentot apron is simply the enormously elongated nymphæ produced by manipulation practised upon the female children from infancy. Elephantiasis vulvæ is a pale or grayish-white tumor arising from any or all of the pudendal structures. It may attain a large size, reaching to the knee. It is composed of fibrous and subcutaneous connective tissue and enlarged and numerous lymph vessels. The surface may be smooth or warty, and when the lymphatic tissue predominates the tumor may present the appearance of a bunch of grapes. Various venereal affections may accompany this condition. The treatment is surgical and consists of radical removal of all the hypertrophied tissue.

Condylomata, or venereal warts of the vulva, present the appearance of warty growths springing from the mucous membrane or from the skin of the vulva. They are auto-inoculable, and may spread on to the mons and down over the perineum and anus, and even on to the thighs. They may be due to simple filth infection of the papillæ of the skin or they may spring from the inflammatory base of a gonorrhœic or syphilitic infection. In rare instances these excrescences become confluent and form large cauliflower-like masses resembling carcinoma. The clinical symptoms and the microscopic examination will give a well-marked differential diagnosis. The treatment consists in their removal either by caustics, by the galvano- or thermo-cautery, or by the scissors. They are apt to bleed profusely when curetted or cut away, and it becomes necessary to touch the base with caustics, with perchloride of iron, or with a strong solution of salicylic acid (℥ i. ad ℥ i.). In some instances it may be necessary to put in catgut sutures to control the hemorrhage.

There are tumors of the vulva which cannot properly be classified as neoplasms, but which nevertheless demand attention here for the purpose of presenting the factors involved in a differential diagnosis. These are intestinal hernia, omental hernia, hernia of the ovary, and cyst of the vulvo-vaginal gland. Intestinal (inguinal) hernia may appear suddenly during a supreme effort at lifting, or as a result of a sudden and unexpected strain, or it may come on gradually. It is usually pyriform with the larger base below, and on percussion it gives the tympanitic note. It may or may not be reducible. Hernia of the omentum gives the same clinical features with the exception of the tympanitic note. Hernia of the ovary is apt to be congenital, but not always. The tumor is small, sensitive, generally irreducible, and it increases in size and becomes painful at the menstrual period. Ovarian hernia occurs also in women whose abdominal walls have been relaxed by frequent and repeated gestation. In these cases the Fallopian tube may be present with the ovary, a coil of intestines and the omentum. The presence of the ovary is manifested by the characteristic dull, sickening pain, aggravated at menstruation to a degree of acute suffering, and by nausea and exquisite tenderness on pressure. In these latter cases the hernia may be reducible, but in congenital cases the ovary is usually fixed.

The treatment of ovarian hernia is surgical, but in all instances, in which this is possible, the ovary should be returned to the pelvic cavity and the hernial opening permanently closed. In exceptional instances, however, extirpation of the ovary is the only resource available, but this must not be undertaken without a recognition of the possibility that it may be the only ovary that the patient possesses, and that the operation is not by any means devoid of risk.

Cyst of the vulvo-vaginal gland is an affection of so great frequency and importance as to demand a separate and independent article (see article on *Bartholin's Gland*, Vol. I., p. 734).

Varicose tumors of the vulva occur frequently during pregnancy. In some cases they cause great pain; in others they burst and occasion serious hemorrhage. Gentle massage and pressure are sometimes efficient in emptying the veins, but the condition may become so extreme, even during pregnancy, as to demand operative procedure. A ligature *en masse* or a mattress ligature may be applied, and the tumor cut away; or the skin may be incised at the base and a catgut ligature applied, after which the skin may be sutured over the stump. Complete asepsis must be observed.

Cancer of the Vulva.—Primary malignant disease of the vulva is comparatively rare. Histologically, it may be epithelioma or sarcoma. Topographically, it may originate in the clitoris, the peri-urethral tissue, the labia, or the perineum. It occurs late in life, with the greatest frequency between forty and sixty years of age. The neoplasms are characterized by a rapid and extensive new formation of tissue and a tendency to early ulceration. The lymph glands, especially those in the inguinal region, are usually involved. The secretion consists of a serous or bloody fluid with a fetid odor. When the peri-urethral tissue is involved the urethra, by vaginal touch, is felt as a round, hard cylinder. The tendency of the disease is to spread internally, the vagina, the rectum, and the bladder being successively involved. The earliest symptom may be a pruritus, but, as the disease advances, the pain becomes increasingly severe. The progress of the disease, if it has not already advanced too far, may be arrested by complete extirpation either with the thermo-cautery or with the knife and scissors. The *x*-ray gives promise of a permanent cure in many of these cases. In those in which ablation is not practicable or the *x*-ray fails to cure, palliative measures consist in thorough and frequent cleansing by douches and antiseptic washes and in the employment of iodoform gauze dressing. The best deodorizers and disinfectants are bichloride solutions, ichthyol, carbolic acid, and formaldehyde. Anodynes are required, both locally and hypodermically, and as frequently and in as full doses as may be necessary to relieve the suffering.

V. Vaginitis.—*Definition.*—Vaginitis is an inflammation of the mucous membrane which lines the vaginal canal. It appears in all grades of severity, from a simple blush of color, with slight heat and dryness, to the most virulent inflammatory action with its attendant constitutional symptoms.

No period of life is exempt from it. It is met with in young girls, in women during the child-bearing period, and in women who have passed the climacteric.

It is most important to distinguish the two varieties—simple or non-specific, and specific or gonorrhœal. They differ primarily in their cause or etiology, and in their remote effects; the one when uncomplicated being attended with only a certain amount of personal discomfort and a limited impairment of general health, while the other may involve, in its later manifestations, serious inflammatory action within the peritoneal cavity—an inflammation which may result in chronic invalidism or even in death.

For convenience of description the subject will be considered under two heads: Simple or non-specific, and specific or gonorrhœal. Simple vaginitis demands consideration under three heads, as it appears: I. In girls prior to puberty; II. In unmarried women; III. In married women.

Vaginitis in Children.—Vaginitis in young girls between the ages of three and seven, and even later, is a very common affection. It usually shows itself in the form of a chronic catarrh. But it may vary in severity from this mild subacute inflammation to one attended with copious discharge and pain, with swelling and excoriation of the labia. The vulva and vagina, as far as can be seen, are sensitive and red, and even the buttocks and inner surface of the thighs may be inflamed and irritated. As a complication in children, it must not be forgotten that gonorrhœal peritonitis is not uncommon, the infection reaching the abdominal cavity through the Fallopian tubes. Forty cases of this character have been collected from the literature. A mistaken diagnosis is apt to be made, owing to the fact that the appendix is naturally involved in the general inflammation. The

condition should be suspected in every case of general peritonitis occurring in young girls between the ages of four and seven, and examination of the vaginal secretions should be made in every case. The prognosis is favorable if the abdomen is promptly opened and the intestines are washed with decinormal saline solution and argyrol (two to five per cent.).

Causes.—It most frequently occurs in weak or strumous subjects, and results from lack of cleanliness. It may arise from "taking cold." In the light of our present knowledge, however, we must understand by this simply a lowering of vitality which affords opportunity for some infectious germs already present to secure a foothold. Seat-worms are a frequent cause, owing to the intense itching they excite, which induces the patient to rub and scratch the parts, usually with dirty hands and finger nails. Or these parasites may find their way into the vagina and inflame the parts by their presence. Self-abuse must also be reckoned among the causes of this disorder and should be ever present in the mind of the physician when he is consulted for this trouble, especially if the case is an aggravated one or persistently does not yield to treatment.

Gonorrhœal poison is also the occasional cause. Dr. J. Lewis Smith records the case of a young man who was under treatment for gonorrhœa, when his two nieces, four and six years of age, respectively, both became infected with specific vaginitis, probably from the towels.

Purulent ophthalmia, which is usually considered the accidental accompaniment of specific vaginitis, may itself be the origin of the vaginal affection. They are reciprocally dependent.

The exanthemata are frequently accompanied and followed by a vaginal catarrh, due either to the direct action of the disease upon the membrane, as occurs in otorrhœa, or to the reduced condition of the vital powers.

Treatment.—The parts should be bathed frequently in warm water and all excoriated surfaces smeared with a protective ointment. Astringent injections thoroughly administered with a glass or hard-rubber syringe are usually necessary, and in some instances must be continued for days and weeks. Tannin or alum solution (five per cent.), sulphate of zinc (two per cent.), nitrate of silver (one per cent.), are all efficient injections and should be administered twice each day. I have found a combination of iron and potash in the usual proportions for a gargle very satisfactory: Tinct. ferri chlorid., ʒ ij.; potass. chlorat., ʒ i.; glycerinæ, ʒ ss.; aq. ad ℥ iij.

When ascarides are present a dose of castor oil should be given, to be followed for several days by daily injections of salt water, lime water, or infusion of quassia, in both rectum and vagina. In the mean time the general hygiene and nourishment of the child, together with appropriate tonics, must not be neglected. Caution must also be given regarding the danger of purulent conjunctivitis and ophthalmia from the infectious discharge. When masturbation is present, of course the child must be put under proper surveillance and restraint.

Vaginitis in Unmarried Women.—Simple vaginitis is rarely a primary affection, being secondary to some inflammatory condition in neighboring organs of the pelvis. As a rule, it begins and continues in a subacute form, but this may at any time take on the character of a violent acute inflammation. On the other hand, the acute form may be excited primarily by some special cause and may gradually pass into the chronic. It is important to determine early in the treatment of the case whether the inflammation be primarily in the vaginal mucous membrane or whether it be induced there by the irritating qualities of a discharge coming from some source beyond the vagina; viz., the cervix, the uterus, the Fallopian tubes, or even a pelvic abscess. Thomas mentions the fact that he has seen two cases of profuse and obstinate vaginal discharge, regarded as the result of vaginitis, which were in reality produced by pelvic abscesses which emptied their contents into the upper part of the vaginal canal. He says: "An element in such cases calculated to mislead the superficial examiner is the fact that vaginitis does really exist to a limited extent as the result of the purulent flow from the abscess."

Etiology.—When the disease is primary, in unmarried women, the most frequent cause is "taking cold." It may arise from undue retention of the menstrual discharge behind a too constricting hymen, where, through contact with the air, it undergoes decomposition and so becomes a source of irritation. Self-abuse is an occasional cause.

Anæmic young women, with a nervous erotic temperament, will often have a constant leucorrhœa with an irritated condition of the vulva and vaginal walls. In these patients the affection is due simply to the vitiated condition of their general health. In our large cities the shop-girls or clerks are the class of patients in which this condition is most often found. The custom of compelling these girls to stand constantly, long hours in succession, in the cramped and narrow spaces behind the counter in crowded stores in which the air is vitiated, produces most disastrous results. Finally, tight lacing, by crowding the viscera down toward the pelvis and by keeping them in a constant state of passive congestion, greatly favors the perpetuation of the disease which we are now considering.

Diabetes is an occasional cause of vulvitis and vaginitis. Accompanying this disease is usually an intolerable itching of the vulva and mons veneris. Through scratching for its relief and the repeated bathing of the labia with urine there is set up an inflammation of the vulva that extends sometimes well into the vagina. It is very intractable, on account of the ever-present irritant.

Vaginitis in Married Women.—In married women, especially those who have borne children, simple vaginitis is not uncommon. In addition to the causes common to all women, as chilling of the body, want of cleanliness, pediculi, ascarides, diabetes, etc., they are much more frequently subject to uterine affections than are the unmarried. Among such affections may be mentioned lacerations of the cervix and the diseased conditions resulting therefrom, the disorders dependent upon rough or excessive intercourse, upon the use of pessaries, which abrade the mucous membrane or simply act as irritants, and upon the accidental contact of irritating substances used for application to the uterus, *e.g.*, chromic acid. Boroglyceride, which is universally employed for saturating vaginal tampons, may, if used in too great strength, not only set up a general vaginitis but cause deep abrasions. The author in consultation recently has had occasion to point out to a colleague the fact that his boroglyceride tampons (fifty per cent. boroglyceride) were the cause of deep and extensive abrasions in the posterior vaginal fornix.

The most frequent cause of a vaginitis is an irritating discharge from the cervix or uterus. In these cases the irritation usually commences at the vulva, where the secretions come in contact with the air, and undergo decomposition, which renders them still more irritating. From this point the inflammation gradually travels back throughout the entire extent of the vagina.

Symptoms and Treatment.—The subjective manifestations vary with the intensity of the inflammation. In very mild cases the patient is conscious simply of a leucorrhœa with slight itching or burning.

A careful examination both by touch and by sight with a Sims speculum is most important. The vagina should be carefully swabbed out and dried with absorbent cotton. By this means the amount and extent of the inflammation can be learned, its primary or secondary nature ascertained, and the cause usually determined. Treatment can then be directed with intelligence and some degree of scientific accuracy. As the affection in this mild form is usually secondary, it demands only palliative treatment, the main efforts being directed to the original cause. Cleanliness and the soothing and astringent effect of heat, both of which are obtained by the hot-water douche, are usually sufficient to relieve

the symptoms. Recovery is hastened by brushing the inflamed tract thoroughly with a solution of nitrate of silver, twenty or thirty grains to the ounce. A vaginitis, it must be remembered, is frequently aggravated and, indeed, sometimes induced, by the poor quality of the glycerin used on vaginal tampons. This is frequently a source of great annoyance, as it is not generally understood.

In an acute attack the clinical features differ very little, and in some cases not at all, from the specific form of the disease. The description of both is therefore embraced in the one account given under the head of Specific Vaginitis. The treatment is also the same for both affections.

Specific Vaginitis.—Synonyms: Gonorrhœa in the female, Gonorrhöe, Vaginite, Blennorrhagie, Blennorrhœa, Elytritis.

Definition.—Gonorrhœa in the female is an inflammation of the genital and urinary passages, characterized by a purulent discharge which has been produced by contact with an infecting substance, as the result usually of sexual intercourse. It may run a very acute course and then become chronic. It may be subacute in its inception, and may slumber in this relatively inactive state for years or until aroused to an acute manifestation by some disturbing element. In an acute case, when first seen, the inflammation is usually coextensive with the entire visible mucous membrane of the genital tract, but it may be limited in extent and confined to the vulva, the urethra, the vagina, or the cervix uteri.

Hardy, Rémy, and, more recently, Bumm, have pointed out the fact that the membrane lining the canal of the cervix uteri may be the original seat of the disease, the virus being absorbed by the cervix directly from the penis during the copulative act. Indeed, the last author maintains that the cervix is, as a rule, the primary seat of all gonorrhœal inflammation. He says: "Gonorrhœa never occurs primarily in the vagina, but usually spreads thence from the cervix, or, more rarely, from the urethra. The stratified pavement epithelium forms so good a protecting tissue that the gonococci cannot effect an entrance unless changes which render the more delicate layers accessible have occurred. Surfaces covered with cylindrical epithelium, viz., the interior of the cervix, are not so resisting."

The frequency with which the cervix is involved and the persistence of the affection in this locality mark it as a most favorable ground for the inception of the disease. The anatomical structure of the mucous membrane, as pointed out by Bumm, makes his *a priori* argument seem reasonable. This view is now accepted by the best observers.

The tendency of the disease, whatever locality it may invade first, is to extend throughout the entire tract of mucous membrane, from the vulva through the vagina, passing through the uterus, into and through the Fallopian tubes to the ovary, and invading the ducts of all the glands opening on all these surfaces.

Sources of Contagion.—There is no doubt regarding the identity of the disease in the two sexes. The gonorrhœal discharge from an individual of one sex, when applied to the genital mucous membrane of the opposite sex, produces a similar discharge, with the same intense and protracted symptoms. But cases occur in men after intercourse with women who, upon subsequent examination, present no sign of the disease. Furthermore, Ricord (and all his host of admirers and followers have insisted on the truth of his statement) declared that a man could acquire gonorrhœa by intercourse with a woman who did not have the disease. At the present time no such belief can be maintained. It seems far more reasonable, in the light of our present knowledge, to believe that, in these obscure cases, the woman, although apparently free from the disease, is in reality afflicted with a latent gonorrhœa.

"True gonorrhœa requires no idiosyncrasy, no ale or champagne, no excess, no weakened condition of the urethra for its development, but simply intercourse with a female [or male] having a gonorrhœal discharge. No abrasion of the membrane is necessary. Simply contact of the virus with the membrane is sufficient to establish the disease" (Van Buren and Keyes).

Latent Gonorrhœa.—The serious nature of gonorrhœa in women and the importance of early recognizing its presence, except for the purpose of avoiding contagion, are matters which have been sadly neglected. The idea of gonorrhœa has been so intimately associated with urethral trouble that unless that particular part of the body was affected no anxiety was experienced. As the acute symptoms rarely continue longer than ten days or two weeks, and then subside without leaving a urethral stricture in their train, this affection in women has been thought a comparatively simple and harmless affair. But since Dr. Noeggerath, in his now classic paper, pointed out the latent propensities of this vicious disease, attention has been more carefully centred upon it, and it is now receiving some of the consideration which its importance demands. The fact is recognized that, after a partial advance toward recovery, the disease may linger for years, and, by gradually extending itself, be the cause of cervical catarrh, endometritis, salpingitis, ovaritis, sterility, and the oft-repeated attacks of peri-uterine inflammation with which its victims are afflicted. But these unfortunate sequelæ not only follow an acute attack in which due warning of their impending arrival has been given, but they may be the first indication of trouble, so insidious is the disease in its latent form.

Dr. Noeggerath's views regarding the frequency of gonorrhœa in women were so extreme, and he insisted so strenuously on sterility as its inevitable consequence, that his paper met with almost universal dissent. This was in 1872. But the pendulum has now recovered its equilibrium, and the careful observer is daily recognizing in his practice cases which illustrate the correctness of the picture which Noeggerath so faithfully drew.

The tenets of Noeggerath's creed are that gonorrhœa, though apparently cured, may exist, in a latent form, in both the male and the female, throughout an entire lifetime; that this latent form may be transmitted to the female, to continue there in a quiescent state for an indefinite period, or, travelling along throughout the mucous tract, excite serious uterine, peri-uterine, or peritoneal inflammation, or at any moment burst forth into acute gonorrhœa. He undertakes to show that the wife of every husband who at any time of his life before marriage has contracted a gonorrhœa is, with very few exceptions, afflicted with a latent gonorrhœa, which sooner or later brings its existence into view through some form of disease of the uterus or its appendages.

While we may not give assent to the universality which Dr. Noeggerath claimed for this form of the affection, it embraces such a large class of cases that it is most important to recognize it, and I cannot do better than place before the reader Dr. Noeggerath's graphic description of a typical case.

"Mr. M——, a merchant of New York, formerly a commercial traveller, like almost every one of his tribe, acquires a gonorrhœa. The treatment recommended by a renowned specialist is carefully followed, and the affection cured in two months. Two years later this gentleman marries a healthy, robust young girl. Three months later the woman begins to complain of backache and general malaise; it becomes difficult for her to attend to the common household affairs; the usual promenade, instead of being a pleasure, becomes fatiguing. Menstruation, which appeared hitherto without any premonitory symptoms, is now connected with backache, more profuse than usual, and followed by a white discharge. By and by the desire to urinate becomes more frequent, and is occasionally accompanied by burning at the meatus. The white discharge gradually extends from one period to the next. About eight weeks later a pain is felt in the left side of the abdomen, which suddenly increases, upon an unusually severe exertion, to such an extent that the patient has to take to her bed. At the same time the dysuria is increased, the discharge becomes profuse and of a greenish-yellow color, like mat-

ter. The physician attending her recognizes an acute attack of perimetritis.

"A year after this she consults me for sterility. I find her suffering from general weakness, backache, pain in the left side, increased before the now scanty menstruation, and a muco purulent discharge.

"On examination the uterus is found in right latero-version and anteflected; the left vaginal roof, or parts above, hardened and contracted; the uterus, soft, succulent, very tender on being gently pushed into its normal position, great tenderness of posterior cul-de-sac, cervix of a high color, surrounded by a thin rim of eroded tissue, discharging a tenacious yellow mucus; both outlets of Cowper's gland eroded to some distance and painful to the touch.

"In the history of this patient we find no trace of the existence of acute gonorrhœa either before or after marriage but a condition very like it, if not truly gonorrhœa, is being developed during the acute attack of perimetritis. The patient has never been infected, in the accepted meaning of the word, but she gradually develops a condition which we usually observe as the result of an attack of acute gonorrhœa."

These cases of latent gonorrhœa are distinguished from simple leucorrhœa in the following manner: If the upper part of the vagina be filled with a copious, glairy, greenish-yellow glue which adheres to the cervix tenaciously when the attempt is made to remove it, gonorrhœa is present. And even when the discharge is scanty, pellucid, white, or of a pale-straw color, it is gonorrhœa, if the five following conditions also exist: (1) If there is also a red, eroded, narrow rim about the os; (2) if there are signs of present or past peri-uterine inflammation; (3) if there is catarrh of the vulvo-vaginal or peri-urethral glands attended with condylomata in the fourchette or around the urethral orifice; (4) if the discharge is very difficult to relieve; (5) if it has developed, soon after marriage, in an otherwise healthy woman, without other morbific cause.

These clinical features are quite sufficient for a diagnosis; but if, in addition to them, the gonococcus be present, the cause of the trouble is at once made clear.

Thus, latent gonorrhœa accounts not only for a large percentage of the manifold troubles embraced under the terms peri-uterine and pelvic inflammation, but there is no doubt that some of the cases of puerperal fever supposed to be due to septic poison are really caused by a latent gonorrhœa; especially those cases in which the inflammation is circumscribed and the general septic condition is absent.

Symptoms.—The patient's attention is early attracted, usually from three to five days after the impure intercourse, by a sense of heat and burning in the vagina. This is followed by aching and weight in the perineum, a throbbing pain through the pelvis, a profuse purulent and offensive discharge, frequent desire to micturate, and swelling of the labia. A severe attack will be ushered in by a chill and sharp rise of temperature—103° to 104° F.,—anorexia, nausea, and general nervous excitation. The mucous surfaces about the vulva become excoriated, and the inflamed parts so sensitive that motion is very painful. If the nymphæ are large they may swell to such an extent as to protrude beyond the labia and become constricted, a condition analogous to paraphimosis.

Accompanying the discharge an almost intolerable itching about the vulva sets in. This is usually worse just when the patient gets warm in bed and wishes to settle down for the night, and it leads her to scratch and tear her person for relief.

As a rule the poison finds its way into one or both of the ducts of the vulvo-vaginal glands, which open just in front of the lateral caruncule myrtiformes. Thence it may invade the gland and set up an abscess. This is extremely painful when once the capsule is put upon the stretch, and continues so until relief is afforded by the bursting of the abscess or by artificial evacuation.

All cases are not so severe. Instances occur in which the redness, swelling, and sensibility are but slight, and the discharge is scant.

Physical Signs.—When the parts are exposed to view, the labia are seen to be swollen and tense, the mucous surfaces smooth and red, or abraded and livid in color; at the same time they are sore and sensitive to the touch. As the labia are separated purulent matter of a creamy or greenish color, sometimes streaked with blood, is seen exuding from the vagina. In the cases which come under observation at the public clinic this discharge may bathe all the external parts, excoriate the perineum back to and around the anus, irritate the integument on the interior aspect of the thighs, and become mingled with the hair of the mons veneris, where it dries in yellowish crusts. The clothes are also soiled and stained with this yellowish discharge. To the touch, when digital examination is possible, the vaginal canal is found to be hot, the papillæ and rugæ rough and prominent. The introduction of the speculum is always painful, sometimes intolerable, and should be managed with great care. When exposed to view through a speculum (and Sims' speculum should always be used in these cases) the vaginal membrane presents a swollen, roughened appearance, the color varying in different cases, and in successive stages of the disease, from a bright red to a deep livid or leathery color, with patches here and there in which the mucous membrane is denuded of its epithelium. These superficial abrasions are found throughout the entire canal, including the vaginal surface of the cervix. About the external os is a ring of inflamed and granulating tissue, and hanging in the os is a mass of muco-pus. If a pessary has been worn, the imprint of it, when removed, still remains in the mucous membrane, and may be marked by abrasion.

The urethra may or may not be involved, the scalding which attends micturition being frequently due to contact of the urine with the excoriated vulva. When, however, the lips of the meatus are swollen and irritated, and pressure by the finger along the canal of the urethra from behind forward causes pus to appear in the meatus after the parts have been carefully cleansed, there can no longer be any doubt about the disease having involved the urethra. Formerly the involvement of the urethra was regarded as a diagnostic sign, but this is not now considered reliable.

Diagnosis.—The differentiation of the gonorrhœal form of inflammation from simple acute vaginitis is extremely difficult, and in some cases impossible, at least by a study of its clinical features alone. If a history of recent suspicious sexual contact or intercourse can be obtained, in conjunction with the well-known clinical manifestations, the question, for all immediate practical purposes, is settled. But final judgment rests absolutely upon the discovery of the gonococcus in the discharges. Microscopic examination must, therefore, never be omitted. In making a diagnosis, and to the same degree in applying treatment, the fact must not be lost sight of that gonorrhœa in woman does not always mean a vaginitis. The two sites of infection that are far more frequent than the vagina are the urethra and the cervix uteri. It is in the secretions from these two sources that the gonococcus must be sought. The secretions of the urethra may be milked out by drawing the finger, with graduated pressure, along the urethra from the neck of the bladder to the meatus. Discharges from the cervix may be obtained by a pipette or on a cotton swab rotated within the cervical canal.

Prognosis.—Can an acute case of gonorrhœa be absolutely cured? There is abundant evidence to prove that cases are so cured, and the physician is justified in assuring a patient that, with proper treatment, the probabilities are that such will be the result in her individual case. But the virus has the property of penetrating so deeply into tissues, and the abundant crypts and follicles and ducts and glands afford so secure a lodging-place for the infectious organism that the question of its total eradication is beyond all ken. The more recent the at-

tack and the more limited the area of infection the more favorable the prognosis.

Treatment.—The importance of stamping out the disease promptly cannot be over-estimated. Whatever line of treatment is pursued must be followed up with the greatest thoroughness, persistence, and attention to detail.

If it be granted that the gonococcus is the causative agent, the use of the most efficient germicide is the indication *par excellence*.

Oppenheimer has made successive experiments to determine which parasiticide is most efficient against the gonococcus. His method of experimentation was to cultivate the gonococcus in sterilized blood serum, the micrococci developing on bits of thread suspended or laid in it. Different substances were then applied to the solution and their effects noted. Alum, bismuth, and acetate of lead were absolutely inert, as were also balsam of copaiba and extract of cubebs. Solutions of bichloride of mercury, 1 in 20,000; carbolic acid, 1 in 20; permanganate of potassium, 1 in 25; weak solutions of nitrate of silver, and a strong solution of either iodine, bromine, or chlorine destroyed the gonococci promptly. Regarding copaiba and cubebs, it is important to state that, by an ingenious experiment, he seems to prove that these substances undergo a chemical change in the system, the products of which change are destructive to the gonococcus. This accounts for the efficiency of these drugs in internal medication.

Conclusions reached by such purely experimental methods must be tested by clinical experience. Nitrate of silver not only acts efficiently in destroying the gonococcus in culture fluids, but is found most satisfactory also in stopping the discharge, relieving the congestion, and restoring a healthy tone to the tissues. Efficient as nitrate of silver has proved as a germicide, it has, when applied to living tissues, the unfortunate property of coagulating the albumin and forming a coating over the epithelial cells. This retards its penetration into the deeper structures and confines its influence to the superficial tissues. Quite recently the pharmacologists have evolved various proteid silver salts. These salts, which contain varying amounts of silver, are known under the following names: argonin, protargol (8 per cent.); albargin (15 per cent.); nargol, argentanin, argyrol (30 per cent.), and many others. Of these, argyrol contains the greatest proportion of silver and is coming into general use. It is highly soluble in cold or warm water and, when applied to inflamed tissues, either in weak or in strong solution, causes no pain or irritation. It does not coagulate albumin or precipitate the chlorides, and therefore is free from any caustic action. Its innocuousness is certified to by ophthalmologists, who assert that it can be dropped with impunity into the eye in strengths of from five to twenty per cent., and that it produces most beneficial results. Moreover, these proteid salts have great penetrating action on vital tissues. A strand of catgut immersed over night in a one-per-cent. solution of argyrol was found to be impregnated through and through with the silver. Fresh stains on linen may be readily removed by hot water, and dry stains may be eradicated by a saturated solution of potassium iodide, followed by hot water.

In all acute cases of gonorrhœal vaginitis it is advisable, if there be no decided contraindications (such as weakness), to administer a purgative dose of calomel, gr. viij.-x., with an equal quantity of bicarbonate of soda, to be followed from time to time by saline cathartics. If the external parts are much inflamed a hot sitz-bath will afford great relief and will produce a tranquillizing effect upon the system.

If the case is seen within forty-eight hours after an exposure, effort should be made to abort the disease. Whenever possible, the patient should be confined to her bed and one of the silver salts—argyrol, for example—should be used freely and persistently. As soon as the parts will tolerate a speculum (and in mild cases this can be done immediately), the vagina should be thoroughly exposed by means of Sims' speculum, all discharge carefully wiped away, and the mucous membrane dried with absorbent cotton. Any excoriated points are to be touched with the stick of nitrate of silver and the entire membrane thoroughly swabbed with a twenty-per-cent. solution of argyrol. It is also well to swab the cervical canal with the same solution. Should the urethra be involved, an applicator moistened with the same solution should be passed into it, or half a drachm of the solution, of the same strength, may be slowly injected into the urethra and held there for from five to ten minutes. These applications may be repeated every second day by the physician, the patient on alternate days taking vaginal douches of argyrol, 1 in 200. At the expiration of from five to seven days the argyrol may be discontinued, and vaginal douches of sulphate of zinc, four to six grains to the ounce, three times a day, may be substituted. At the same time capsules of santal oil and balsam of copaiba, ãã. gr. v., should be administered by mouth. At the end of ten days the secretions should be carefully examined. If no diplococci are present, the patient may discontinue treatment and be pronounced cured.

If leucorrhœa occurs later, or if bladder symptoms arise and gonococci appear, the disease must be considered chronic and a regular siege begun. If the cervical glands are involved, the entire cervix may be reamed out or amputation performed. Before resorting to so radical a measure, it may be wise thoroughly to dilate the cervix with the steel dilator from time to time, and then to apply argyrol. The dilatation expresses the secretions from the ducts, crypts, and glands, and permits of a more efficient diffusion and penetration of the medicament. If the infection travels into the body of the uterus it must be followed by thorough swabbing of the endometrium with argyrol. The wisdom of employing curettage under these circumstances is questionable. The ducts and glands of the endometrium are more shallow and simple than those of the cervix and hence more amenable to the effect of the application, while curettage may open lymph spaces to the infection and thus permit it to advance beyond the reach of the germicide. If the infection reaches the uterine appendages, it may be limited in its extension and severity by making an opening at once into the cul-de-sac of Douglas and inserting an iodoform drain. Unless general peritonitis threaten, no radical operation should be instituted till the pus has become circumscribed and the acute symptoms have subsided. The pus becomes sterile in the course of a few months, and then ablation can be performed with comparative immunity; or, in the course of a few years, conservative work may be done successfully upon the appendages.

Argyrol is also the best remedy to apply to the bladder when a cystitis develops as a complication. It may be used daily in the strength of from five to twenty per cent. The urine should first be drawn and then the bladder slowly distended with the injection, to the fullest degree of toleration (fifteen to twenty ounces). A long-standing urethritis may result in a urethro-vesical fissure, causing frequent and painful micturition and tenesmus. Dilate the sphincter vesicæ with the steel dilator, apply argyrol, and afterward administer urotropin, gr. x., night and morning. In persistent cases it may be necessary to resort to an artificial vesico-vaginal fistula, for the purpose of affording rest to the parts and thus permitting them to heal.

The patient and attendants must be cautioned about the contagious nature of the discharge, especially the danger to the eyes. All cloths and napkins used about the patient should be burned or at once soaked in strong bichloride solution. In the mean time the patient must be kept in bed, if possible; the diet should be light, simple, and nourishing; she should drink plenty of milk and avoid all spirituous or malted liquors.

When an anodyne is necessary, chloral may be tried, or, better still, opium may be administered in the form of a Dover's powder or in that of a suppository containing either opium or morphine.

The pruritus is at times the most difficult symptom to

relieve. The most efficient application is carbolic acid, which can be used in the strength of a five per-cent. solution, although it is well to commence with a weaker solution and increase the strength if necessary. The parts thus affected may be brushed with a solution of cocaine or of the nitrate of silver; both are efficient.

Should one of the vulvo-vaginal glands become involved it will be necessary to open it as far within the vaginal outlet as possible. This condition may be mistaken for a prolapsed ovary or an inguinal hernia. The former is excluded by the previous history and the latter by its percussion note and, possibly, by reduction. The opening of the abscess will afford temporary relief; but when once this gland has been invaded, it becomes a source of frequent annoyance, and a permanent relief is obtained only by its complete eradication.

Buboes are not apt to occur. When they are present, an effort should be made by purgatives and counter-irritants to dispel them. A grateful application consists of an ointment composed of equal parts of Ungt. hydrarg., Ungt. belladonnæ, ichthyol, and lanolin. Apply with pressure. If suppuration is inevitable dissection alone affords the desired relief.

Granular vaginitis and adhesive vaginitis are described by some authors as distinct forms of inflammation. They also occur as phases of simple or gonorrhœal vaginitis, and hardly demand special consideration. The former, however, sometimes declares itself as a distinct form of vaginitis in connection with pregnancy.

VI. Vesico-Vaginal Fistulæ.—A fistula is an abnormal communication through the tissues between two organs or passages, or between an organ or passage and the exterior of the body. The course of the communication may be either direct or tortuous. A vesico-vaginal fistula is such a communication between the bladder and vagina; by means of it the urine constantly or spasmodically makes its escape.

These urinary fistulæ are classified according to their location as follows: I. Vesico-vaginal fistula (proper). This is situated in the vesico-vaginal wall and involves only that tissue. II. Vesico-utero-vaginal fistula. This comprises cases in which the tear reaches up to, or dissects off the vesico-vaginal tissue from, the uterus, and necessitates, when an attempt is made by surgical means to repair the defect, the passage of the suture through uterine tissue. III. Vesico-uterine fistula. In these cases the vaginal wall is intact, the bladder communicating with the uterus and the urine thus finding its way through the os into the vagina. IV. Urethro-vaginal fistula. This term is applied to cases in which an opening exists in the base of the urethra, through which urine escapes into the vagina. But this can occur only during the act of micturition. V. Uretero-vaginal fistula. This is the rarest form of fistula. It is the result of an extensive tear or loss of tissue involving the ureter. Dr. Emmet claims that this lesion is more commonly the result of a pelvic abscess. During the inflammatory process the ureter becomes occluded by pressure, perforation ensues, and the urine finds its way into the vagina. A uretero-vaginal fistula may be congenital, and cases are on record in which one ureter opened into the vagina and the other took the normal course and discharged the urine from one kidney into the bladder. Under these circumstances a diagnosis becomes obscure and difficult. During infancy and childhood simple incontinence suggests itself as an efficient explanation of the apparent phenomena, and repeated physical castigation is apt to be the lot of the unfortunate sufferer. It is only when the child has come to mature years that a sufficiently thorough investigation is instituted and the exact condition discovered. Congenital ureteral fistulæ usually open at a point below the neck of the bladder. Uretero-vaginal fistulæ occur not uncommonly from accidental wounds of the ureter in hysterectomy for cancer or for fibroid tumor of the uterus.

The most common location of a vesico-vaginal fistula is in the median line and directly behind the symphysis pubis. The usual form of a section of the fistula is oval, linear, angular, or round. The most common is the oval, due, as Dr. Agnew explains, to the superior contractile power of the longitudinal over the circular muscular tissue of the vagina. These fistulæ vary in size from an opening so small that it is found with great difficulty and admits only the smallest probe, to those that involve the whole of the anterior vaginal wall, together with the entire base of the bladder and the urethra. One illustration of the latter has come under my own observation and care. In this case there was no trace of urethral tissue whatever. The entire base of the bladder was wanting, and, stretching across the common cavity, behind the symphysis, and springing from and continuous with the tissue of the recto-vaginal septum, was a strong cicatricial band which reached from side to side of the pelvis, leaving only sufficient room for two fingers to pass with difficulty between it and the symphysis. Through this small opening the inflamed and sensitive fundus of the bladder frequently prolapsed. Such cicatricial bands, of greater or less density and resistance, and reaching across the vagina in the most diversified directions, are a common complication in cases of fistula.

Etiology.—The most common cause of urinary fistula is injury due to parturition. If the delivery be premature and rapid, especially when attended with undue rigidity of the soft parts, laceration of the cervix uteri is apt to occur. Especially is this the case in primiparæ of advanced age, and in cases in which morbid changes have occurred in this tissue. When sufficiently extensive this laceration results in a permanent fistula. The vesico-utero-vaginal and the vesico-uterine are the varieties most often produced in this way. The tear, beginning in a rigid os, extends out upon the vagina or up the cervix to the vesico-cervical junction. In the process of repair this may all heal with the exception of an opening at the junction of the vagina with the cervix. Or all the tissues below may heal, leaving an opening at the upper angle of the tear—a vesico-uterine fistula.

It is universally accepted now, however, that the majority of fistulæ are caused by the sloughing away of tissue due to severe and prolonged pressure of the presenting part of the child during parturition. So long as the pressure is intermittent, and not too long sustained at any one time, no harm is done; but when impaction occurs and the pressure becomes continuous, circulation is obstructed and the vitality of the soft tissue thus compressed is destroyed. Necrosis occurs, the slough separates, and the urine makes its escape. According to Agnew, over ninety per cent. of vesico-vaginal fistulæ are thus produced, while in Emmet's experience ninety-five per cent. of his cases were the result of prolonged and difficult labor.

When the fistula is produced by laceration the urine makes its escape at once and the condition is immediately suspected. But in cases of protracted labor time is required for the slough to separate and the urine may not escape for several days. The average time is ten days, but it may occur in four or five, and again it may be delayed for a month. One case under my care gave a history of retention of urine, following confinement, that persisted up to the ninth day, when suddenly her bladder burst and a flood of urine was discharged through the vagina. It was evident in this case, however, from the presence of cicatricial bands, that there had been some sloughing as a result of the pressure, and that the separation of the necrotic tissue had led to what she described as the "bursting of her bladder."

Ill-adjusted, displaced, and neglected pessaries have been known to ulcerate through the vaginal wall and produce fistula; vesical calculi likewise may ulcerate through into the vagina, leaving a fistulous opening. Urinary fistulæ are sometimes produced by gunshot wounds, by rough manipulation of a sound or catheter in the bladder, by accidental puncture during operations on surrounding tissue, as in the operation for atresia vaginæ or in amputation of the cervix uteri in malignant disease, etc. Contrary to former teaching, malignant dis-

ease of the uterus in itself almost never produces a vesical fistula. The essential tissue of the bladder is so highly organized, so well nourished, that it is enabled to resist the encroachments of such morbid action. As has been said, however, fistulæ are not infrequently produced in the course of operations for the relief of such troubles.

Occasionally cases of congenital fistula present themselves, but they are rare. The same methods of relief apply to them as to other cases; but at an early age the parts are usually too small to permit of successful operation.

Frequency of Fistula.—No statistics can be given showing the frequency of this accident. I have no hesitancy, however, in saying that it is a rare condition, and, if the experience of New York gynæcologists is an index of the experience of practitioners throughout the country and the world, it is becoming more and more infrequent. The Woman's Hospital, in New York City, was established primarily for the express purpose of relieving fistulæ, and its early history bears record of few cases of a different nature. During the first five or six years of its existence it was customary to have two or three operations each week for the relief of fistulæ. At the present time scarcely that number can be seen there in a year.

This change is due to two causes: First, the operation has become so popularized that when such an accident does occur, the local physician repairs the injury; second, the prompt application of forceps in cases of difficult labor prevents the damage to the tissues which otherwise would be likely to occur. Whatever abuses and injuries may attend the too frequent and too early use of forceps in parturition, all authorities are now agreed that their timely use is most efficient in preventing fistulæ. "Authors are disposed to attribute the accident of vesico-vaginal fistula in many cases to the awkward use of obstetric forceps; but from a careful analysis of these cases, and my own experience, I am well satisfied that for one case thus produced their judicious application has prevented it fifty times" (Sims). "I do not hesitate to state that I have never met with a case of vesico-vaginal fistula which, without doubt, could be shown to have resulted from instrumental delivery" (Emmet).

Symptoms.—In cases in which the bladder is punctured by an incised wound, the fact is at once made known by an immediate and involuntary escape of urine through the puncture. The same phenomenon indicates the presence of a fistula caused by laceration, due to too rapid delivery, or by ulceration due to the pressure of a pessary, calculus, or any foreign body in the vagina. This escape of urine may be continuous from the date of its first appearance, or may be interrupted. But as the vast majority of fistulæ are due to prolonged and difficult labor, the usual symptoms are those that follow such an experience. The presence of bruised and sloughing tissues furnishes a warning of the more serious condition to follow. But the actual extent of the injury cannot be known until the slough separates and the urine escapes by the fistulous opening thus established. This may occur on the third day, and may be delayed until the third week. From this time on, the urine may flow constantly, or may be retained for several hours, according to the position of the patient and the nature and seat of the fistula. If the lesion is high up in the septum, the bladder will have retentive power until it becomes filled up to that point; and when the patient is in an erect posture there will be no involuntary escape of urine if the bladder is evacuated frequently enough to prevent the overflow. Sometimes a fold of the vagina, the pressure of the uterus, or the approximation of the edges of the fistula, especially in fissure-like openings, may afford retention for hours. In uretero-vaginal fistula, when only one ureter is involved, there may exist the unusual condition of an almost constant dribbling of urine from the vagina with occasional normal micturition. Unless the woman devotes almost her entire time and efforts to personal cleanliness, the mucous and cutaneous surfaces over which the urine flows soon become inflamed and excoriated. The vulva, the thighs, and the nates, being kept constantly wet with this irritating excretion, become red, swollen, and abraded. Frequently they are the seat of vesicles and pustules, and even occasionally of deep ulcerations and abscesses. Such abrasions within the vagina soon become coated with a calcareous or phosphatic deposit that causes the greatest suffering. When there has been an extensive loss of the tissue of the vaginal wall the base of the bladder may become inverted through the opening. Under these circumstances it is just as likely, as in the condition just described, to undergo abrasion, and to become coated with a deposit, both of which alterations render it exquisitely sensitive. Otherwise the size of the fistula makes little difference with the discomfort of the patient. A woman may be as constantly wet when the opening is not larger than a pin's head as when it is large enough to admit one or two fingers, the small opening, as Dr. Emmet explains, acting like the spigot in a barrel. A disagreeable urinous odor is constantly emitted from her person, a circumstance which excludes her from society and forbids her participation in the ordinary pleasures and duties of life. Dieffenbach gives a sad picture of many of these unfortunate women of his time, shunned by their friends, disgusted with themselves, and dragging out a most pitiable and miserable existence.

Diagnosis.—When the symptoms above described exist, the probabilities are that a urinary fistula will be discovered. Sometimes, however, a chronic cystitis will result in paralysis of the bladder and constant dribbling of urine from the urethra, producing all the disagreeable symptoms of a fistula. If the fistula is larger, a digital examination will readily detect the lesion without the use of speculum and probe, but pinhole openings are sometimes most difficult to discover. In long-standing cases of extensive lesions, with abrasions and cicatricial bands, the true relations of the parts are discovered only by careful and painstaking investigation. When the opening is very minute, the whole field of the vagina must be gone over carefully with tenaculum and probe. The folds of the vagina are smoothed out and the probe is gently insinuated into every suspicious lead or fissure. Should this fail to reveal the fistula, resort can be had to injecting milk, or water stained with indigo or cochineal, into the bladder. A simple method consists in administering by stomach methylene blue, gr. iss., night and morning. This will give the urine an indigo-blue color and will promptly reveal the point of escape through the vaginal wall. In carrying out this method it is necessary that the bladder be allowed to become slightly distended with the chosen fluid, while the septum is carefully watched for its appearance upon the vaginal wall. Bozeman has devised an ingenious test for cases in which the previous methods are contraindicated by reason of the irritability of the bladder. The test is based upon the fact that urine instantly passes through linen, while secretions of the vagina do not. The suspected location of the fistula is carefully dried with absorbent cotton, a piece of thin linen is spread smoothly upon it, and carefully watched for the point of moisture to appear.

Prognosis.—In artificial fistula, made for the relief of calculus, or an obstinate cystitis, it is a well-known fact that it is with difficulty that the fistula can be kept open long enough to effect a cure. Not until Dr. Emmet devised his method of "working the buttonhole," was this difficulty obviated. In these cases the fistula is a simple slit or fissure, the edges of which fall naturally together when the speculum is removed. We may, therefore, infer that where the lesion consists of a laceration in the vesico-vaginal septum, due to rapid labor or accidental puncture, unless it be so situated that the natural strain of the parts tends to keep the lips of the wound apart, under proper attention to cleanliness and frequent emptying of the bladder, spontaneous recovery may be hoped for. Even when a slough has occurred, spontaneous recovery has taken place in a limited number of cases. In the majority of instances, however, the lesion becomes permanent and requires surgical interference for its relief.

"Prior to the application of the metallic suture by J.

Marion Sims, and a proper mode of exploration furnished by his speculum, any attempt for the relief of the injuries under consideration was uncertain in result, and the operation regarded as an opprobrium by the profession." To appreciate fully the significance of these words of Dr. Emmet, and the credit due to Sims, it may be interesting and profitable in this connection to look into the history of the treatment of the lesion under consideration.

History of the Different Operations for Vesico-Vaginal Fistula.—With Henri de Roonhuysen—a Dutch obstetrician of Amsterdam (1663)—rests the honor of being the first to devise, employ, and describe an operation for the relief of vesico-vaginal fistula. The description which he gives is so unique and interesting, and so rarely to be found, that I give it in full. This is from a French translation of the original by Herrgott, of Strasburg. The operation is done in the following manner: The patient is placed upon her back on a table, in a good light; the upper part of the body is covered, the lower part fixed with bands as in the operation for cystotomy. This done, the vagina is dilated by a speculum as large as the circumstances will permit. The vaginal mucous membrane along the border of the tear, where it is in contact with the vesical membrane, must be denuded, but the bladder itself must be touched as little as possible, for by the kindly act of nature the vagina is united by inflammation to the borders of the tear in the bladder in such a way that, when only as little a portion as necessary has been denuded, it is wont to heal perfectly. This freshening (of the edges) can be done by means of a little sharp pinch of the scissors or bistoury, or any other instrument the surgeon is in the habit of using. I find that it is accomplished quite well by a slight, sharp pinch of the scissors, but they ought to be as sharp as possible in order that they may not produce contusion, but freshen a little the edges of the tear to make them red or bleeding, so that they may unite immediately and contract adhesions to each other. The retention need not always be accomplished with gold or silver pins, as is done in harelip, but with pins made from the strong quills of the swan, sharpened and pointed. These are preferable, not only by reason of their flexibility, but on account of the fact that they do not cause contusion of the surrounding parts if one takes the precaution to guard them with waxed silk. For when the pins are applied they adapt themselves by virtue of their elasticity. The parts must then be anointed with a cicatricial salve (of which he gives the formula), and upon the wound should be placed two or three flat pledgets saturated with oil or warm balsam, and the vagina filled with pieces of sponge saturated with oil, for the purpose of making a little pressure upon the wound and of sustaining the dressing. All this should be steadied with some compresses and supported by a T-bandage, which should remain in place three or four days. The bandage and compresses are removed when the patient wants to urinate, but she ought to do it with caution. The patient should remain constantly in bed, lying upon her back, the hips slightly elevated, until healing is accomplished.

Roonhuysen does not describe cases operated upon by himself, nor does he state how many times he practised the operation; but a Swiss surgeon, J. Fatio (1752), records two successes by Roonhuysen's method. Naegele claimed that this procedure of Roonhuysen was simply impossible, basing his objections upon the quill pin, but he nowhere claims to have tried it. Kilian made similar objection to the operation. But Herrgott has experimented with quill sutures in tissue similar to that of the vagina, and finds them entirely practicable. Moreover, the minute and careful description of all the details of the procedure bears evidence in itself of being a genuine account of what had actually been done.

In this simple description of Roonhuysen's we find all the principles and methods of treatment necessary for dealing successfully with fistulæ. He used the speculum thoroughly to expose the parts, vivified the edges of the fistula with knife or scissors, avoided the bladder membrane in denuding, and fastened the edges with a suture. What have we added to this more than to modify the suture and adjust a self-retaining catheter?

The method, however, was not established, either by him or by any of his immediate followers, as a recognized procedure in surgical practice, and was forgotten. Aside from the use of the catheter by Vorlten (1720) and the introduction of silk interrupted sutures, no progress in dealing with fistula was made during the eighteenth century. Cauterization of the edges with the hot iron and with nitrate of silver was used, but with only limited success. In the beginning of the last century Naegele (1809) renewed interest in this lesion and its repair. He devised and employed four methods of operation, but failed to obtain any success. Professor Ehrman (1826) operated in two cases by simple suture after freshening the edges, and obtained complete success in one of them after repeated cauterizations.

Gosset, of London (1834), reported a successful case operated upon by him, in which he used uninterrupted sutures of silver gilt, or gilded silver wire, fastened by twisting. Jobert de Lamballe, the same year, in France, introduced the method of transplanting tissue from the labia, the buttocks, or the thigh, and fastening it to the denuded edges of the fistula. This did not prove satisfactory in its results, and he adopted the interrupted suture with the additional procedure of incising the tissues at certain points in the vagina—cystoplastie par glissement—to relieve tension upon the sutures and allow the edges to rest in contact.

Then Dieffenbach (1845) gave his experience to the profession. He says: "I have operated upon one woman eighteen times without success. I have closed the entire cavities of these unfortunate women gathered from all countries. I have lived in the midst of them, and I have realized only a small number of successes." He claimed to have cured by the suture only one fistula of any considerable size, but a great number of small ones by the actual cautery.

Wurtzen, of Bonn, who after Dieffenbach was for a long time the only one who operated upon fistulæ, failed to cure in one case after thirty-three operations. According to the statistics of Simon, Wurtzen, up to 1842, cured only 4 women out of 18. From 1842 to 1852 he cured 7 out of 17, or 11 successes in 35 cases.

Gustave Simon (1854), published a critical review of the operation of Jobert in which he presented his own method of operating, and reported six cases in which he had obtained perfect success in four, and partial success in the other two.

In our own country, Hayward, of Boston, was the first to report a cure, May 10th, 1839, achieved by him in a case of fistula of fifteen years' standing, which had resisted treatment by cauterization and the use of the catheter. He operated with the patient in the lithotomy position, the vagina being opened by means of retractors, and the anterior vaginal wall being pressed down by a bougie in the bladder. The edges were denuded, the surfaces coaptated by interrupted silk sutures, a catheter was fastened into the bladder, and the patient put to bed upon her right side. Upon the sixth day firm adhesion had taken place and the stitches were removed. He says: "I had never seen the operation done till I did it myself, nor could I find any description of the mode which others had adopted that was sufficiently clear and explicit to be of much service." In 1851 he reported a series of 20 operations on 9 different patients, with 3 perfect successes, 4 great relief, 2 no benefit. Of these, 5 had 1 operation, 2 had 2, 1 had 5, and 1 had 6.

In 1847 Pancoast, of Philadelphia, reported two cures by a method called his "plastic suture." The peculiar feature of this consisted in splitting one edge of the fistula and paring the other to a wedge shape. The latter was then slipped into the former and held by sutures. The same year, 1847, Mettauer, of Virginia, reported a successful case of fistula treated by him with leaden sutures after freshening the edges. He also used the catheter. So simple seemed the process of cure, and so pro-

nounced his success, that he did not hesitate to declare that all fistulæ are susceptible of relief.

From this brief historical sketch it becomes apparent how perfectly at sea the profession was, even as late as the middle of the last century, regarding any well-established procedure, and how little faith it had in the successful application of any of the devices used. Here and there, occasionally, an operator met with success, and the achievement was heralded as a great triumph. But no two adopted exactly the same method, and the success was ascribed more to good luck than to the proper application of any particular surgical method. It was left for the genius, the careful observation, the untiring energy and enthusiasm of one of our own countrymen, J. Marion Sims, to grasp all the essential principles, to work out to complete success, and give to the profession, what is recognized the world over as a thoroughly reliable method of dealing with urinary fistulæ in women. The more credit is due him as he worked independently of others, and without any adequate knowledge of what had been accomplished by them. Yet, as Dr. Emmet says, "were we assured that Dr. Sims was as familiar as we are at the present time with what had been accomplished before his day, it should not lessen the credit due to him. What had been done fell on barren soil, bore no fruit, was not appreciated, and was destined to be forgotten. From Dr. Sims' hands the operation was accepted by the profession; it was immediately put into successful practice, and to the present day it has not been materially modified for the better, either in its principles or in its mode of execution." His first article was published in the *American Journal of the Medical Sciences*, 1852. The essential features of the procedure, as there set forth by him, were, first, suitable means by which the vagina could be thoroughly explored and the fistula brought into view—viz., the knee-chest posture and the duck-bill speculum; second, a suture which could be left in place long enough to secure healing without exciting inflammation or ulceration — viz., silver wire secured by perforated shot; third, a method of draining the bladder during convalescence—Sims' self-retaining catheter. During the next five years he modified somewhat the details of these proceedings, and set them forth in an address before the New York Academy of Medicine, in 1857, on "Silver Sutures in Surgery." In the operation as then described, one which he regarded as perfect in all its details, he substituted the simple interrupted silver suture, secured by twisting, for the clamp suture, and, instead of the knee-chest position, employed what is known universally as the Sims posture.

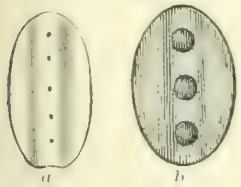

FIG. 4946.—The Lead Button.

While Sims was thus perfecting the details of his operation, Gustave Simon, of Darmstadt, Germany, was also employing his mechanical skill and ingenuity in endeavors to relieve the same distressing affliction. The results of his labors, and the details of his operation, were given to the profession in 1862, although he had previously published an article on the subject in 1854. He placed the patient in an exaggerated lithotomy position; exposed the fistula by a duck-bill speculum of his own device; and, by means of lateral retractors, vivified the edges with a knife, regardless of encroachments upon the bladder membrane, and used silk sutures in uniting the edges. When much strain was expected, he employed a row of deep sutures far from the edge to hold the parts, and a row of superficial sutures to obtain nice approximation of the edges. He allowed his patients to sit up and pass urine naturally, when possible. Simon also devised and practised what he called kolpokleisis, in cases in which the fistula itself could not be closed. This consisted in completely occluding the vagina by denuding a surface on the anterior wall of the vagina below the fistula, and a similar one on the posterior wall, and uniting them by suture. This made a common receptacle for the urine and menstrual blood, all of which was passed through the urethra.

Intimately associated with the operation for repair of fistulæ, both in this country and abroad, is the name of Bozeman. He is a strong advocate of long and complete preparatory treatment and of the use of the button suture. The latter consists of a strip of sheet lead nicely cut and moulded to fit the tissues in each individual case. This is perforated, along the median line, with a row of holes (Fig. 4946, *a*) through which the silver sutures are drawn and made fast by perforated shot (Fig. 4946, *b*). This, it is claimed, acts like a splint, and so favors healing by preventing motion. It has the disadvantage, however, of concealing the wounds, preventing the nice adjustment of the edges, and of tightening or loosening each individual stitch, opportunities for doing all of which things are afforded by twisting the wire. He employs a peculiar speculum invented by himself (Fig. 4947), and a contrivance for sustaining the patient in the knee-chest posture when under ether.

His method yields most favorable results in his own hands, but is too complicated for the general practitioner.

Dr. Bozeman is a vigorous opponent of the operation of kolpokleisis as practised by Simon. He claims that in many cases in which this was resorted to by Simon, a sufficiently long and persistent course of preparatory treatment would have enabled the patients to be relieved, with entire restoration of bladder and marital functions. Kolpokleisis, even in cases that resist all other efforts at relief, is only a delusion. It may keep the patient dry, and thus afford relief for a short time; but unfortunate consequences always attend the retention of urine in a pouch thus formed when complete drainage is not secured. The urine decomposes, calculi form, and a cystitis may be established that, sooner or later, leads to disease of the kidneys, uræmia, and death. Dr. Emmet insists that kolpokleisis should never be resorted to under any circumstances.

The man who, while claiming no originality in the matter, has done the most to popularize the operation for fistula in this country, is Dr. T. Addis Emmet.

Treatment.—Methods of Cure. Spontaneous Cure. Small fistulæ will frequently close without any interference, through the processes of granulation and healing. The smaller the fistula the greater the probability of such an occurrence. This process of nature can be encouraged and hastened by proper attention to cleanliness. The constant drainage of the bladder, too, by a self-retaining catheter, assists greatly this spontaneous cure. Any procedure that maintains a constant healthy, granulating process along the edge of the fistula tends to the accomplishment of a cure. Corradi cites a case of his, recorded by Jenks, which for a year had resisted all methods of treatment, even Sims' operation. He thereupon had a gold button with double facets made to fit

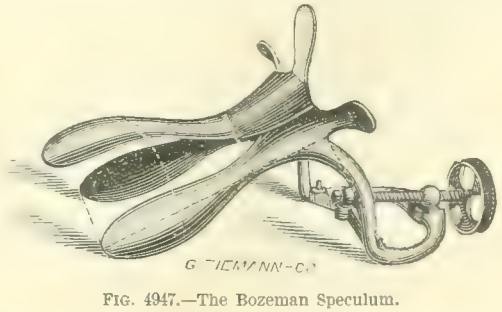

FIG. 4947.—The Bozeman Speculum.

the fistula. The button was inserted so that one facet was in the bladder, the other in the vagina. Micturition was immediately established, and not a single drop of urine passed any longer by way of the vagina. For five years the woman wore this button without experiencing any inconvenience. Then by accident the button dropped

out, and the urine continued to pass entirely by the urethra. A few days afterward Corradi examined the patient, but found no fistula. In this case the stimulus of the button had encouraged granulation till it had reached up over the head of the facet that was in the bladder, while the button was sloughing out below.

Caustics.—For many years caustics were the chief reliance in the cure of fistulæ. As late as 1839, Dupuytren declared that sutures were of no avail against the injurious influence of the urine on the wound, and nothing but the actual cautery was sufficient to excite the necessary degree of granulating activity in the edges of the fistula. All the caustic acids, caustic potash, nitrate of silver, and the actual cautery were employed. In cases of extremely small fistulæ the actual cautery will frequently effect a cure. Among the caustics of a chemical nature nitrate of silver is the best. It is used not only as an independent means of causing a fistula to heal, but also for the purpose of completing the cure after suture, when an opening has been left in the angle, or when points along the line of union have failed to unite. In such cases the silver should be applied frequently and its use should be continued until strong, healthy granulations have been produced. After that, cauterize less frequently; allow the granulations to accomplish what they can before burning them again.

DETAILS OF THE OPERATIONS.

Preparatory Measures.—It is important that the general health of the patient should be in as good condition as may be. But one need not wait too long for this. The local condition of the parts is still more important. Before operating, the edges of the fistula and surrounding parts must be put into as healthy a condition as possible. Sitz-baths, hot-water douches, and the most scrupulous methods of personal cleanliness should be employed. All incrustations of urinary salts, whenever found, are to be gently removed by streams of warm water or by a cotton swab, or they may be picked off with the dressing forceps. The excoriated surface beneath is then brushed over with a solution of nitrate of silver. This preliminary treatment must be repeated two or three times a week, and in the mean time the parts should be kept thoroughly protected from the urine by an ointment. The most efficient ointment for this purpose is that given by Bartholow, under the head of Boracic Ointment. "Take of boracic acid, finely levigated, 1 part; white wax, 1 part; paraffin, 2 parts; almond oil, 2 parts. Melt the wax and paraffin by heating with the oil, and stir the mixture briskly, along with the boracic acid powder, in a warm mortar, until the mixture thickens." When it is required for use, a certain amount of it should be rubbed up with a little vaseline or glycerin. It should be used quite stiff, so that it may form a coating over the inflamed and delicate surfaces. With careful attention to cleanliness and the constant use of this ointment, I have kept patients with artificial fistulæ entirely free from abrasions, excoriations, or irritation.

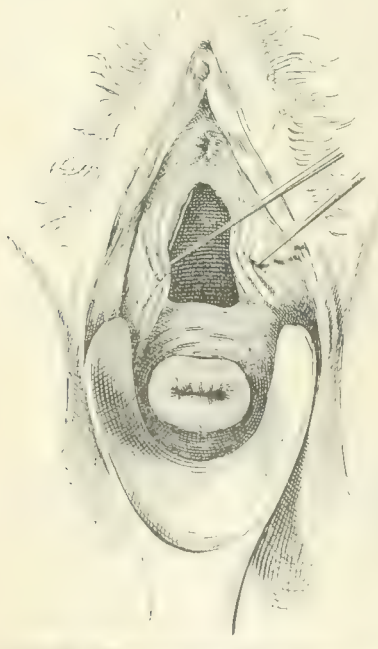

FIG. 4948. Fistula as shown by Sims' Speculum.

All cicatricial bands that stretch across the vagina, obstructing the view and narrowing the canal, or distorting the relations of the parts, must be thoroughly obliterated. This is accomplished by nicking or cutting them here and there along their course and causing their absorption by pressure. When these constricting bands exist across the posterior wall, reaching up on to the sides of the vagina, they can be put upon the stretch by placing one or two fingers in the rectum and the thumb in the vagina. Then, with a pair of blunt scissors in the right hand, each band is snipped or cut superficially at several places, and the pressure of the thumb increased to tear the tissue still deeper. By adopting this plan one may avoid the hemorrhage that would be produced by the deep incisions of a knife. When the bands cannot be reached in this way, a speculum must be inserted and pressure made here and there with a depressor to bring the bands into view. When once they have been revealed, they may be snipped by the scissors in the manner already described. To keep these bands on the stretch and stimulate absorption by pressure, a "Sims glass plug," or a "Bozeman dilator," should be inserted immediately after they have been snipped, and these contrivances should be held in place by a layer of cotton and a T-bandage. This plug or the dilator can be procured of any size, and must be adapted to each individual case. It should be large enough to distend well the parts. Its presence occasions some distress, which may be relieved by anodynes. During the

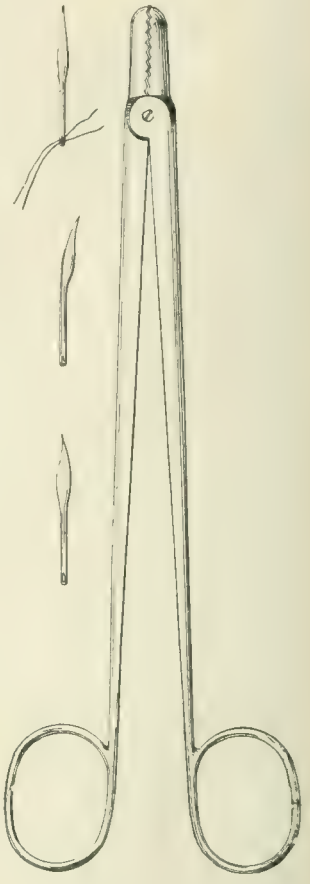

FIG. 4949.—Needle-holder and Different Patterns of Needles.

FIG. 4950.—Emmet's Needle-holder.

healing process the patient is kept in bed, and the plug kept as constantly in place as the circumstances will permit. It should be removed at stated intervals to permit the use of carbolized douches, and it should be well smeared with carbolized vaseline before being reintroduced. At the expiration of ten days or two weeks, if the parts are not sufficiently pliable and the vagina is not roomy enough to permit the easy performance of the operation, the process just described is to be repeated.

If cicatricial bands do not exist, but the canal is narrowed through loss of tissue, and if the edges of the fistula are so drawn apart that they cannot be brought into apposition, longitudinal incisions, three or four in number, parallel to the long diameter of the fistula, should be made through the mucous membrane of the vagina with a knife, and the dilator or plug then inserted as described above.

FIG. 4951.—Sims' Fork.

FIG. 4952.—Twisting-tongs.

FIG. 4953.—Shield.

Sometimes this becomes a very painful and tedious process. A much more satisfactory method consists in splitting the edge of the fistula throughout its entire extent and dissecting the bladder wall free from underlying tissue widely in every direction until the edges of the fistula in the bladder wall can be readily approximated. Then the vagina should be incised longitudinally on each side, to remove undue tension, and afterward the edges of the fistulous opening should be stitched together—the edges of the bladder wall first and those of the vaginal mucous membrane afterward. The wounds left by the lateral incisions may be allowed to heal by granulation.

Sims' Operation.—The patient, properly dressed and protected by covering, is placed in Sims' posture. It is well to have two nurses and two assistants. One nurse holds the speculum and elevates the buttock; the other attends to the sponges. One assistant administers ether; one assists in the operation and does the sponging. The instruments required are: silver wire, twisting tongs, wire shield, sponge-holders, and sponges (see accompanying cuts).

The steps in the operation can be comprised under three heads: First, denuding or vivifying the edges of the fistula; second, introducing the sutures; third, adjusting the edges and fastening the sutures.

Denuding.—The line of union should be, as nearly as possible, in the long axis of the vagina; but more important still is it that the margins be drawn together in the line of least traction or resistance. The margin of the fistula is caught with a tenaculum at any selected point, and a strip of tissue is removed with the scissors or knife.

It is a good plan to make this strip of tissue encircle the entire fistula without cutting or breaking it. Then you are sure of obtaining a perfectly clean surface. When the vesical mucous membrane is included in this denudation there is apt to be troublesome hemorrhage. Sims therefore advised that this be carefully avoided; the incision taking the direction of the dotted lines, as in Fig. 4957, *a* being the vesical mucous membrane and *b* the vaginal. If the removal of one strip gives a surface wide enough to afford firm union, the wound is ready for the sutures. Ordinarily, however, it is necessary to take off a second or third strip outside this, on the mucous membrane of the vagina, in order to get as broad a surface of union as may be. At each end of the fistula the denudation must be made to terminate in an acute angle by extending the denudation out to a point on the vaginal membrane. This prevents all puckering of tissues when the sutures are tightened; it also diminishes the likelihood that any little orifices will be left at either end of the line of union. Should any troublesome hemorrhage occur, it can usually be controlled by adrenalin or by hot sponges, torsion, pressure, or ligature. To exert pressure, Dr. Emmet recommends pushing the centre of a handkerchief of gauze or cloth through the fistula, then packing cotton into the sac thus formed in the bladder till the mass is too large to be drawn through the opening. After this

FIG. 4955. Denuding with Scissors.

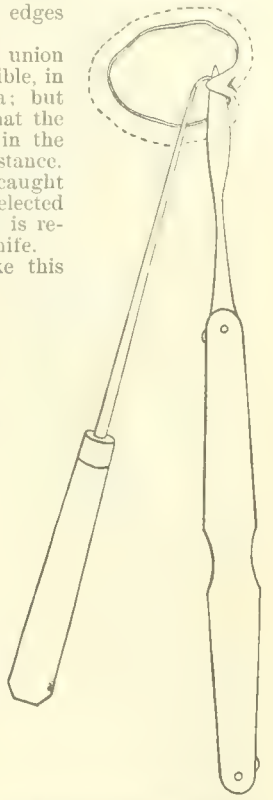

FIG. 4956.—Denuding with Knife.

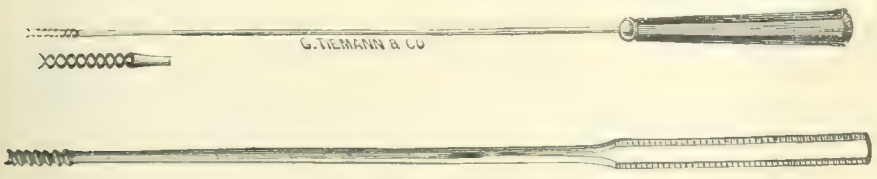

FIG. 4954.—Sims' Tampon Extractor, with closed and open screws. (After Mundé.)

Sims' speculum, long-handled left and right curved scissors (Emmet's cervix scissors are usually sufficient), a long-handled knife with narrow blade, two or three tenacula, needles and needle-holder, counter-pressure hook and fork, twisted silk for carrying No. 27 or 28

has been done, it will be found that, by pulling on the corners of the handkerchief, any degree of pressure can be made. Another of Dr. Emmet's devices is to pass a suture from the vagina through the septum into the

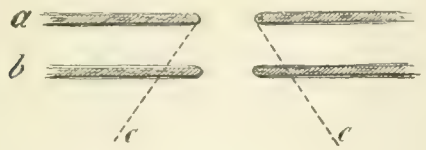

FIG. 4957.—Showing Direction of Incision (viz., that of dotted lines ending at *c*).

bladder, at some distance from the margin of the fistula, and out into the vagina again, thus surrounding the offending vessel, and ligating it temporarily in the tissues. Care must be taken in doing this to avoid ligating a ureter. If the mouth of the bleeding vessel can be caught, there is no positive objection to ligating with fine silk or with catgut; but the leaving of any foreign body between the lips of the wound is to be avoided if possible.

Introducing the Sutures.—The needle may be either straight or slightly curved, and from one-half to one inch in length. It is armed with a double carrying thread of fine silk about six inches long, into which the silver wire of the same length is hooked and made fast. The wire should be sharply bent over the thread in order that, when it reaches the tissues, it may be forced through them (by the aid of the forceps) with the minimum amount of difficulty.

It is well to begin suturing at the proximal angle of the fistula. Here the tissue is caught up with a tenaculum and the needle inserted at about one-fourth of an inch from the margin of the denudation, and directed through the tissues so that it will come out just at the edge of the mucous membrane of the bladder.

Puncturing the vesical membrane causes hemorrhage at the time, and may result in a permanent leak hole. As soon as the point at which the needle is to emerge is determined, counter pressure is made just beyond with the blunt or counter-pressure hook. This facilitates the passage of the needle and prevents straining of the tissues. The needle is thus pushed through as far as the grip of the needle-holder will allow. Then it is caught at the point and drawn through while the counter pressure is still applied. The needle is then inserted at the point corresponding to its exit on the edge of the mucous membrane of the bladder, on the opposite side of the fistula, and directed through the tissues till it makes its appearance through the vaginal mucous membrane one-fourth of an inch from the margin of the fistula. The counter pressure is applied as before. The needle, with carrying thread and silver wire, is now drawn through till the ends of the wire can be grasped on both sides. If the tissues are delicate and there is

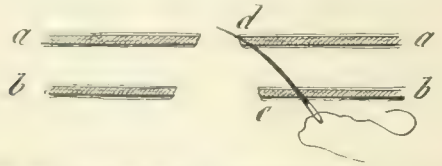

FIG. 4958.—Showing Direction in which Needle is to be Passed. *a a*, Bladder membrane; *c b*, vagina.

danger of tearing them, it is well to support the thread, as it is drawn through, with a Sims fork. But the wire must not be drawn into the tissues till the needle has been passed through both sides, and then it is to be slid through both sides at the same time; otherwise it is likely to get badly kinked. The ends of the wire are twisted together one or two turns and held out of the way by the assistant. In this way the stitches are passed one after the other from one-fourth to three-eighths of an inch apart, and as evenly in all respects as it is possible to get them.

Securing the Stitches.—Commencing now at the remoter angle of the fistula, the surgeon should grasp firmly both ends of the first wire, two or three inches from the tissues, with the twisting-tongs, and he should make the tension sufficient to draw the suture taut. With slight pressure of the tenaculum the wire of either side is now bent, near the tissues, at a sharp angle, till it meets

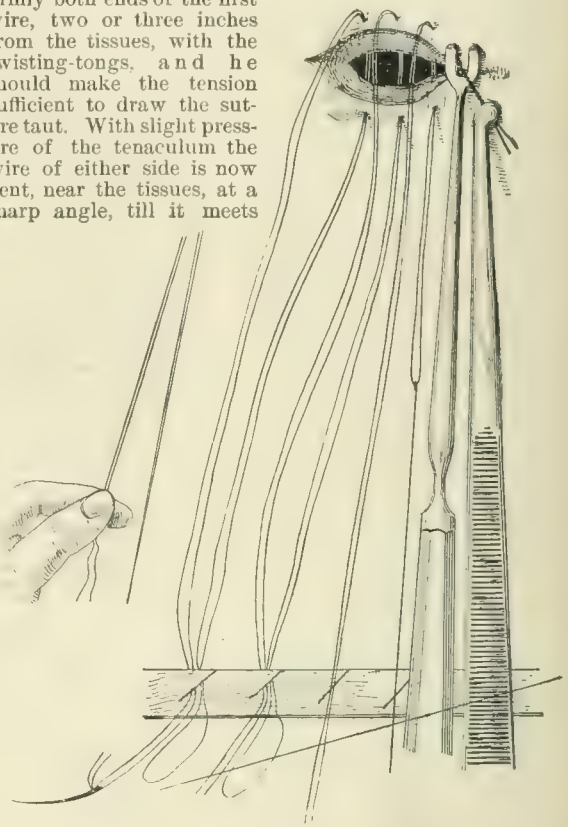

FIG. 4959.—Twisting the Wires. (Savage.)

the wire of the opposite side directly over the line of union that is to be formed. The shield is then slid down the wire and firmly pressed against the tissue, while sufficient strain is put upon the wire, by pulling, to bring the edges of the wound into firm apposition. While this tension is still maintained, the wire is bent over the shield and twisted down to the tissue. (Fig. 4959.) The shield is now removed in order that the operator may see whether this suture holds the edges in close and exact apposition. If it does not so hold them, the shield is reapplied and one or two more twists are given to the wire. Or, if the twisting has been carried too far and strangulation or cutting of the tissues threatens, the tension can be relaxed by giving the wire one or two turns in the opposite direction. And in this lies the advantage of securing silver wire by twisting rather than by clamp, button, or shot.

FIG. 4960.—Adjusting the Wire.

The sutures are now shouldered by catching the loop of the stitch with a tenaculum at the point of exit from the tissue, and pulling at a right angle to the line of the fistula, first on one side and then on the other, so that the wire shall be bent at a right angle where it comes out of the tissue, and shall lie flat across the face of the wound.

The twisted end is next bent at a right angle over a

tenaculum, flat upon the vaginal membrane, and cut off so that it shall have a length of about half an inch. It is customary to turn the twisted ends alternately to one side and to the other.

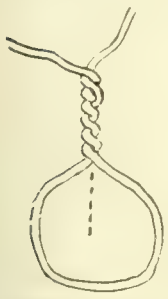

Fig. 4961.—Stitch before Shouldering. (Munde.)

When the sutures have all been disposed of successively in this manner, the wound should be thoroughly inspected, all everted points should be carefully tucked in with a tenaculum, and all inverted points of mucous membrane should be turned out. This completes the operation. But before the patient is removed from the table the bladder should be carefully inspected by passing a catheter. If any blood clots are discovered they must be dissolved by normal saline solution and washed out; if there is any active hemorrhage it must be controlled by applications of either hot water or ice-water or by injections of adrenalin.

The self-retaining catheter is now placed in position, and the patient put to bed with a narrow dish between her thighs to catch the urine. The catheter should be removed and thoroughly cleansed every night and morning, and a vaginal douche administered at least once a day. The bowels may be kept constipated till after the fifth day, or an evacuation may be obtained daily by Hunyadi water or by some other laxative. It was Dr. Sims' custom to keep the bowels quiet. The patient is kept upon her back, and pain is relieved by opium or by morphine. The sutures may be removed upon the eighth, tenth, or twelfth day, according to the relative vitality of the patient and the healing qualities of the tissues.

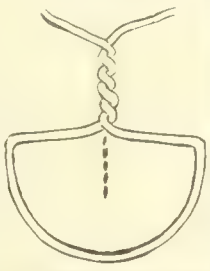

Fig. 4962. Stitch after being Shouldered. (Munde.)

Care must be exercised not to pull the wound apart in removing the sutures. Catch the twisted end with the twisting-tongs, and straighten it up gently to a right angle with the surface. While this is being done, the loop of the suture will rotate in the tissues and bring a bright point of it into view, when it can be easily snipped with wire scissors. The view is facilitated by making slight pressure on the tissues with the points of the scissors at the point of exit of the suture. In drawing the suture out, the surgeon should direct his force in such a way that the tissues shall not be constantly pressed toward the line of union, nor dragged away from it.

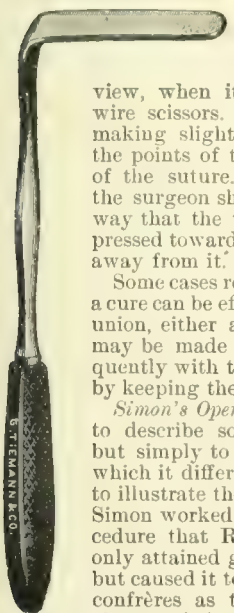

Fig. 4963.—Simon's Retractor.

Some cases require several operations before a cure can be effected, but slight points of non-union, either at the angles or along the line, may be made to heal by touching them frequently with the stick of nitrate of silver and by keeping the catheter in the bladder.

Simon's Operation.—It will not be necessary to describe so minutely Simon's operation, but simply to speak of the main points in which it differs from the Sims operation, and to illustrate them by the accompanying cuts. Simon worked along the same lines of procedure that Roonhuysen described, and not only attained great success in his operations, but caused it to be adopted among his German confrères as the standard operation. The characteristic features of Simon's operation are these: First, he employs an exaggerated lithotomy position, patient on back, hips elevated. Second, instead of avoiding the vesical mucous membrane, he intentionally incises it if the edges contain much cicatricial tissue. Third, he repudiates the superiority of silver wire and uses silk. Fourth, he employs no stationary catheter, and allows the patient to void her urine if possible. Fifth, the bowels are kept in a relaxed state to avoid straining, the diet is not restricted and the patient is not necessarily confined to bed.

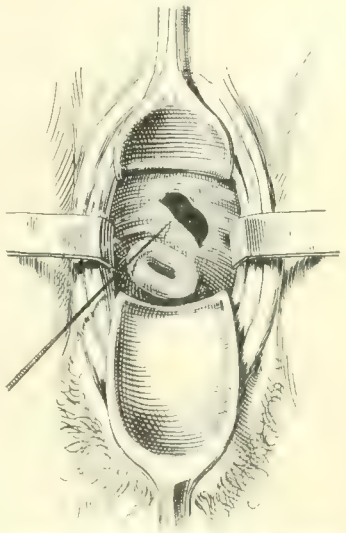

Fig. 4964.—Fistula as shown by the Goffe or by Simon's Speculum.

Position of the Patient.—The breech-back (Steiss-Rückenlage) position is attained by elevating the hips and flexing the legs over the belly, so that the breech becomes the most projecting part. If the fistula is situated high up in the vagina, the hips must be well elevated, and the thighs flexed as much as possible. The lower the fistula is situated in the vagina, the less the degree of elevation and flexure necessary. Whenever it is possible to expose the fistula well by traction upon the cervix, either by forceps or by threads passed through, the speculum is dispensed with, and only side retractors are used, with a staff introduced into the urethra to steady the parts. When this is not practicable Simon uses specula devised by himself. These consist of an anterior and a posterior speculum, and two side retractors (Fig. 4963).

Vivifying the Edges.—The Simon method carries the incision deep enough to extirpate all cicatricial tissue, making a funnel-shaped excavation, and includes all the tissues down through the vesical mucous membrane. Simon prefers the knife.

Sutures.—When the fistula is small a single line of silk sutures is used. In the larger fistulæ every second or third stitch is made a sustaining suture, and is passed at a considerable distance from the edge, thus including enough tissue to support the line of union and take the strain off the more superficial (uniting) sutures. This Simon called his double line of sutures. It is of very little importance whether the sutures go through the vesical membrane or not, but care must be taken to prevent the membrane being inverted and caught between the edges of the wound.

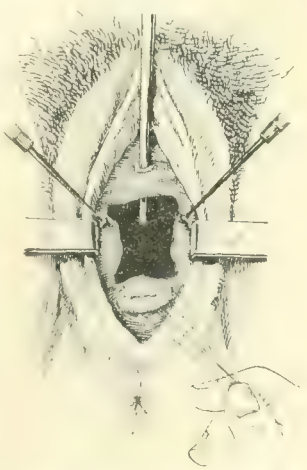

Fig. 4965.—Fistula shown with Retractors and Staff. (Simon.)

After-treatment.—The patient takes any position in bed that she desires. She passes urine normally whenever she feels the desire, either lying upon a bedpan, sitting up, or getting on the hands

and knees. If urination is impossible without too much straining, the catheter is passed at proper intervals. A daily vaginal douche is given, and the bowels are kept open. Vesical tenesmus is relieved by sedatives. Silk sutures cannot be left as long in place as silver wire; they should be removed at some time between the sixth and the eighth days.

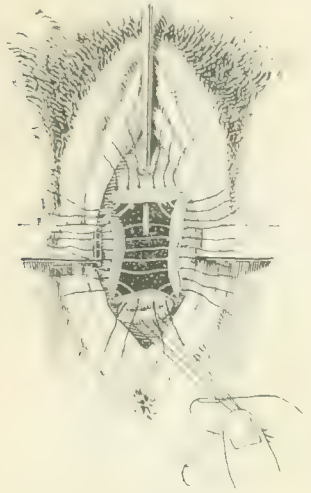

Fig. 4966.—Sutures in Place. (Simon.)

General Remarks.—The principles and methods established by these two great teachers, Sims and Simon, can be followed successfully in all cases. Succeeding operators have modified many details, or have combined into a successful procedure some of the features of each. Each operator follows his own fancy in regard to the needle or the needle-holder which he shall use, and the material of which his ligatures shall be made. Chinese silk, silver wire, iron wire, silkworm gut, and chromicized catgut are used indifferently; but in large fistulæ, and those so situated that they cannot be reached easily for fastening the ligatures, silver wire is preferable.

There is no department of plastic surgery which gives so great scope for the ingenuity of the operator as that of vesico-vaginal fistulæ. Each case is a problem *per se* and demands its own special and individual treatment. No case should be undertaken without careful study of all the factors that are involved in its successful treatment. The modern methods of vaginal section have led to greater freedom in incising the vagina for the purpose of reaching for operative purposes the tissues beyond, and they have demonstrated the feasibility of dissecting freely the vaginal sheath from the bladder, thus giving direct access to the bladder wall. Acting upon this principle, the author has devised the following method of dealing with vesico-vaginal fistulæ, whether large or small, and wherever situated:

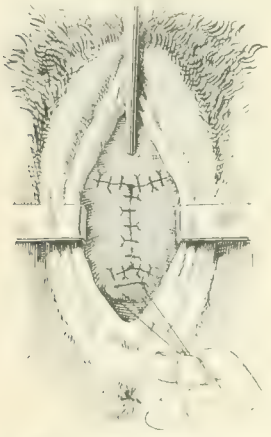

Fig. 4967. Lines of Sutures to close the Fistula shown in Figs. 4965 and 4966. (Simon.)

The Author's Operation. — Vesico-vaginal fistula is best treated by separating distinctly the vaginal wall (and that includes the vaginal sheath, or fascia, as well as the mucous membrane) from the wall of the bladder, so that the two distinct openings can be closed separately, each in its own way. The operation consists of three distinct steps: First, incising the vagina down to the wall of the bladder by a longitudinal incision reaching, in the median line, from the cervix to the neck of the bladder. A transverse incision, reaching well across the vagina, is next made in front of the cervix; then afterward the bladder is to be separated from the vagina well out beyond the location of the fistula on whichever side of the median incision the fistula may be located, or if the fistula is in the median line the separation should extend on both sides sufficiently far to set the bladder wall free for some distance beyond the borders of the fistula. In extensive fistulæ it may be necessary to dissect the entire bladder quite free from all its attachments, not only for the purpose of bringing the fistula within the reach of surgical procedure, but also to remove all strain upon the tissues. The third step consists in denuding the edges of the opening in the bladder and closing it with one or two tiers of chromicized catgut sutures, care being taken not to pierce the vesical mucous membrane. After this has been accomplished the orifice in the vagina may be denuded and closed, and the vaginal incisions sutured. If the fistula involves the ureter, it can be easily and efficiently dealt with after the separation of the vesico-vaginal septum.

In cases that involve loss of tissue at the lower portion of the vagina, extending to one or both rami of the pubis, there may not be enough tissue between the fistula and the bone for the passage of the sutures. In such cases the tissue can be dissected up from the bone to a sufficient extent to give holding ground for the sutures, or a flap may be dissected off the vagina above and brought around to cover the opening. Jobert was a most skilful operator in the use of flaps, which he procured from other portions of the vagina, from the labia, or even from the buttocks and thighs.

Fig. 4968. The Goffe Speculum, made in two sizes.

In vesico-utero-vaginal fistulæ, where such a course is practicable, only the anterior lip of the cervix uteri should be utilized in closing the opening; but in some cases it is found necessary to stitch the posterior lip to the anterior border of the fistula, thus turning the os uteri into the bladder. Menstruation then occurs through the bladder and conception, as a rule, becomes impossible.

In vesico-uterine fistulæ, Dr. Emmet boldly slits up the cervix till he reaches the fistulous opening, thus, as he claims, reproducing the original lesion The fistulous tract is then denuded and the entire wound closed by sutures, as in trachelorrhaphy. Uretero-vaginal fistulæ are perhaps the most difficult to deal with. Landau recommends excising an oval piece from the vesical and vaginal wall, thus producing a vesico-vaginal fistula into the upper angle of which the ureter opens. Then the fistula is to be closed by sutures which, at the upper angle, shall include only the vaginal mucous membrane. If the urine is successful in forcing its way into the bladder in spite of the partial constriction of the ureter which may occur from the stitches, it will continue to do so. There is no danger of occlusion by the presence of granulations, for the flow through the ureter is constant. Another device for securing a patulous condition of the ureter is to introduce an elastic catheter from the vagina into the ureter, and then to pass the lower end out through the bladder and urethra. The uncovered portion of the catheter, as now seen through the vagina, is to be covered with the vaginal mucous membrane and the lower ureteral wall.

If a vaginal operation has failed or it seems useless to undertake such an operation, then resort must be had to

ureteral cystotomy through an abdominal incision. (See also the article on *Ureters. (Surgical.)*

Occasionally a patient presents herself in whom there has been such extensive loss of tissue that all hope of closing the fistula must be abandoned. The question of closing the vagina (kolpocleisis) then arises. This is to be adopted with great hesitation. Indeed, in this country, the experience of the best operators is opposed to it. Continence of urine may be obtained, but, as has been previously stated, it is only at the risk of constant vesical tenesmus, calculus, and chronic cystitis, with all its train of direful consequences. When the base of the bladder, filled with intestines, becomes inverted and protrudes at the vulva, Emmet recommends that enough of the sides of the vagina be united, as in kolpocleisis, to give needed support, but that an opening be left at the most dependent point to allow of free drainage. By proper attention to cleanliness and the use of rubber urinals for females, which can now be procured at the instrument-makers, the patient can be made very comfortable.

VII. Tamponing the Vagina.—Custom has established the use of two words to signify the placing of cotton, wool, or other similar substance in the vagina—viz., tamponing and tamponade. Tamponing signifies the complete packing of the vagina for the purpose of stopping or preventing uterine hemorrhage; tamponade is used when a limited amount of cotton or other similar substance is employed for purposes of medication.

The Tampon.—The use of the tampon originated in the idea of placing something in the vagina to facilitate the formation of a clot. It was first practised by loosely stuffing in a handkerchief, napkin, roller bandage, or a few wads of cotton. Such tampons are more or less effective in stanching temporarily the external flow of blood. But in a short time the tampon becomes saturated and hemorrhage again becomes apparent.

To Dr. Emmet we owe the thorough and efficient method of tamponing the vagina as it is now used, or should be used. His method is based on the idea of pressure. And while the stoppage of all hemorrhage depends upon the formation of a clot, the pressure thus produced carries the uterus high up in the pelvis, compresses all the pelvic vessels, thereby diminishing the blood supply, and transfers the formation of the clot from the vagina up into the uterus.

To tampon the vagina properly a Sims speculum is indispensable. As Mundé ("Minor Surgical Gynecology") very forcibly remarks: "Every practitioner who takes, and is liable to meet with, cases of uterine hemorrhage (and what practitioner is not?) from miscarriage, polypi, polypoid endometritis, fibroid uterus, or cancer, should not only possess a Sims' speculum, but should know how to use it and how to tampon the vagina so securely that not a drop can escape so long as the tampon is retained."

When the hemorrhage is free it may be necessary to tampon the cervical canal as far as the tampon can be forced into it. This will prevent the escape of blood from the uterus, and the blood, in turn, by accumulating and forming a clot within its cavity, stimulates the uterus to contract and so control the hemorrhage. There is no danger of the uterus enlarging to accommodate the clot as it increases in size, except directly after delivery, and when this is to be feared other methods of inducing contraction of the uterus must also be resorted to—*e.g.*, ergot, applications of cold, pressure through the abdominal wall, constitutional stimulants, etc.

If there is reason to believe that the hemorrhage is produced by something within the uterus,—as, for example, a retained placenta, or a polypus, which can be removed at the time,—this indication, as a matter of course, is to be acted upon first. But frequently these cases of hemorrhage occur in the night, or some other reason for delay in operating exists, or the patient may be so reduced that the first indication may be to prevent further loss of blood. Under these conditions resort must be had to the tampon.

The best material for the tampon is plain sterilized cotton, non-absorbent, squeezed out of carbolized water, and flattened out into discs one-half the diameter of the palm of the hand and about one-half inch thick. Non-absorbent is better than absorbent cotton, as it retains its elasticity and so, by its expansile power, increases the pressure. It is well to have, in addition, five or six tampons that have been squeezed out of alum water, of the strength of an ounce to the pint. These are the first to be used about the cervix and fornix vaginæ.

The bladder must be emptied either naturally or by catheter, and, if the case is not too urgent to permit time for it, the rectum should be unloaded by enema. The patient is placed in the Sims position, the Sims speculum is introduced, and the cervix is brought well into view. All coagula and fluid blood are wiped away with absorbent cotton held in dressing forceps, and the vagina is hastily swabbed out with bichloride solution, 1 in 5,000. If the os is patulous and the hemorrhage free, it may be well to pass the applicator, wrapped with absorbent cotton and dipped in iodine, as far up as to the fundus. If a decided impression on the uterus seems necessary, the cotton can be slipped off and left in the uterus as the applicator is withdrawn; but care should be taken to leave the end of it protruding from the os. The uterus will be stimulated by this means to contract, and probably to force out the cotton. In some cases one or two small plugs can be packed into the cervix. This will assist materially in stanching the flow of blood.

One of the disc-shaped tampon balls is now placed over the os, another posteriorly to the cervix, one on either side, and one in front. These are not rolled up into balls, but are spread out and moulded to the vaginal fornix by pressing them all about with the dressing forceps in the right hand, and a stiff probang stick, or another pair of closed dressing forceps, in the left. This completes one circle or layer of the tampons. Another layer is to be placed upon this in the same way, the discs being crowded well in against the cervix until the fornix is filled out flush with the external os. Disc after disc is thus placed around the cervix in a circle and well packed down. Each disc inserted is held in place by the rammer in the left hand until the next one can be inserted; in this manner the pressure is at no time relaxed. As the walls of the vagina stretch, and the diameter of the canal increases, a circle of discs is placed around the central one; then another concentric circle is placed outside of that, and so on until the vaginal wall is reached, the pressure being always made at first toward the centre. But as the lower section of the vagina is reached all the pressure is made toward the hollow of the sacrum, the final discs in each layer being tucked in against the anterior vaginal wall. The whole process is similar to that employed by a dentist in filling a dental cavity with gold leaf. No great force is used at any time in the proceeding; but, by firmly packing down each disc of the elastic cotton, the vagina can be gradually distended, if necessary, until the tampon nearly fills the entire calibre of the pelvis.

At first, the point of the speculum should be directed well toward the back, and then, as the work of packing advances, the end of the instrument should be allowed to slip along the floor of the pelvis. Sometimes the space thus left by the speculum can be filled in with two or three extra discs. Upon finally removing the speculum great care must be exercised not to dislodge the tampon.

When the vagina is thus packed there is no possibility of any further hemorrhage. The amount of cotton used and the thoroughness with which it is packed must vary with individual cases. A slight degree of pressure is sufficient in some cases, and the extreme degree of thoroughness alone suffices in others. It is necessary in all cases to confine the patient to bed, and when the tampon is large an anodyne is required. The pressure is especially painful about the neck of the bladder, and, if this persists in spite of the anodyne, some of the discs in this region can be removed at the end of an hour or two without impairing the integrity of the tampon. When such removal becomes necessary there is usually retention

of urine and the patient has to be relieved with the catheter.

The tampon should not be allowed to remain longer than twenty-four hours. At the end of this time it has usually become soaked along one side, at least, with the bloody secretions. It is then more or less offensive and must be removed. It may be that it has done its work and is no longer necessary; in any event, it has ceased to be of use and should be replaced by a fresh one.

FIG. 4969. Tampon Pledget

It is most advisable, as recommended by Mundé, that the surgeon should keep on hand, in a well-stoppered bottle, a supply of absorbent cotton which has been soaked in some styptic solution—*e.g.*, subsulphate of iron (one part to three of water) or alum (one part to twelve)—and allowed to dry. This can be applied directly to bleeding surfaces, as in cancer, before one proceeds to the application of the tampon.

If Sims' speculum is essential to the placing of the tampon, Sims' screw tampon extractor is quite as important for its removal. By means of this instrument the first few pieces of cotton are removed without the use of the speculum. The external parts are separated by the left hand, and the screw, guided along the finger, is screwed into the discs, and they are removed one by one till the pressure is somewhat removed from the perineum. Then the speculum is introduced a short distance, and, as fast as the cotton is removed, it is slid farther and farther in until, with the final emptying of the vagina, it will have reached the farther end of the canal. In removing the tampon pledgets great care must be exercised not to overlook one, especially about the cervix or interior of the uterus. When so overlooked they are apt to be the cause of septic infection, occasioning a chill, rigors, and a rise of temperature.

Tamponade.—The tamponade is not so formidable an affair. It is in constant every-day use for the treatment of all kinds of uterine difficulties. It is employed for various purposes, the most important of which have been enumerated by Mundé under eight different heads, as follows: (1) As a carrier for the application of medicinal agents to the cervix and vagina; (2) as a means of retaining certain substances introduced into the uterus in their proper position—such as pledgets of cotton, tupelo tents, stem pessaries; (3) as a means of retaining the uterus or a prolapsed ovary in position; (4) as a mechanical support and stimulus to the pelvic vessels and as an alterative to the pelvic tissues by means of pressure; (5) as a protective to the ulcerated, inflamed, or swollen cervix or vaginal walls, to prevent friction and an increase of irritation; (6) as a means of dilating or separating the vaginal walls—a substitute for a hard or distensible dilator—in constriction of the vaginal canal after operation for vaginal atresia or stenosis in vaginismus, and in spasm of the levator ani muscle; (7) as a hæmostatic (I have already considered this subject under the head of *Tampon*, but there is another use of the tamponade or tampon that I deem worthy of special mention, and therefore shall consider it as the 7th, viz., to hasten expulsion in unavoidable miscarriage); (8) as an absorbent of vaginal and uterine discharges, which are thus prevented from touching the external or sound parts, and as a protection of the sound parts from caustic substances applied to the uterus or cervix.

FIG. 4970.—Cylindrical Pledget.

This procedure has its special indications in the application of caustics, such as chloride of zinc, to malignant disease of the cervix or vagina. One or two tampons saturated with the caustic are applied directly to the diseased area, and are then kept in place by one or two dry tampons, after which the healthy portions of the vagina and the external parts are protected by tampons wrung out of a saturated solution of sodium carbonate and packed in the canal in such numbers as to fill the rest of the vagina.

As a carrier of medicinal agents the tamponade has come into almost universal use. The best material is the sterilized non-absorbent cotton or wool. The absorbent cotton, plain or borated, is extensively used. But when saturated with glycerin or moistened with the vaginal discharge it packs together too solidly, and has no elasticity. The absorbent cotton is used mainly as a mop in the dressing forceps for cleansing and drying out the vagina, and as a vehicle, when wound on an applicator, for making intra-uterine applications or for painting the vaginal vault.

Other materials besides cotton are used at times by the medical practitioner. Chief among them are tow, marine lint, wool, oakum, sponges. Of these the sponge is the least desirable. On the other hand, the cotton fulfils every purpose, is easily procured, is cheap, and, in fact, is the most generally used.

FIG. 4971.—Proper Application of Cotton Pledgets. Ordinarily only two are necessary, viz., the one posterior to the cervix and the one next to it. (After Mundé.)

If some disinfectant, as carbolic acid, boroglyceride, or iodoform, is always used in the material with which the pledgets are loaded before being applied, the cotton needs no further preparation than to be made up into tampon balls ready for use. These tampon balls should not be made with too great nicety as regards looks. They pack together better and so retain their place in the vagina better if they are somewhat irregular in outline. The best way is to pull or tear off the cotton from the end of the roll, without unrolling it or removing it from its wrapper, in little masses of varying size, about two inches long and an inch thick, and without folding in the edges any more than enough to secure it all with the string. When this string has been made fast to it the tampon will be ready for use. (Fig. 4969.) The purpose of the string is to enable the patient to remove the tamponade herself. It should be long enough to project well out of the vagina, and strong enough not to break when traction is made upon it. For this purpose the neatest and simplest material to use is Clark's white cotton thread, No. 12 or No. 14. When used double it is sufficiently strong to withstand any strain that may be required. A convenient way is to cut off the thread about fourteen inches long; then catching it by the middle point, pass the two strands around the pledget, slipping them through the loop and drawing it up tight enough to hold the cotton securely. It is time-saving to make up a supply of these at convenient moments or to have the nurse do it. A number of these pledgets are saturated with the medicament from day to day, according to the number to be used, and kept securely covered to avoid evaporation.

The old-fashioned kite-tail tampon was made by tying a number of pledgets one after the other on a string. This was easy of removal, and in that respect was a suc-

cess; but it was apt to get badly tangled and was awkward to handle.

Foster's lamp-wick tampon was a great improvement on this, and is an excellent device. The ordinary old-fashioned lamp-wick, as it comes wound in balls, is the material used. It is cheap, elastic, and absorbent; is readily introduced and has the merit of being as easily removed by the patient. Usually a single strand of the wicking is tucked into the vagina through a speculum; but when the ostium vaginæ is capacious several coils of the wicking may be gathered into wads and inserted one after the other without breaking the strand. When enough has been introduced the wick is cut off at the vulva, leaving the end thus protruding. To remove it the patient pulls on the projecting end and thus unwinds the mass within the vagina, drawing it through the vulva in a single strand.

Medicinal Agents.—Glycerin is the medicament most generally used on the tamponade, and with it are combined alum, ichthyol, fluid extract of eucalyptus, boroglyceride, carbolic acid, boracic acid, according to the indications. The tampon pledget may be dusted with a dry powder, bismuth, alum, tannin, or iodoform, or it may be smeared with an ointment. One or two medicated pledgets are to be inserted, and these are held in place by one or more dry ones.

It is important to bear in mind, in using the tamponade, that the patient must be informed that she has a specified number of pledgets of cotton in her vagina, and instructed how to remove them. The custom is to remove the tamponade at the expiration of twenty-four, thirty-six, or at the most forty-eight hours. No sudden traction should be made upon the thread lest it break. It must be drawn steadily downward toward the perineum, and when any astringent has been used on the pledget it is well to instruct the patient or nurse to pass her finger into the vagina alongside of the cotton and allow a little air to enter as the pledget is withdrawn. Otherwise the cotton acts like a piston in a pump, and may drag down the tissues above, even to the extent of retroverting the uterus. Passing in the syringe tube alongside of the cotton and injecting a little water will also prevent this unpleasant occurrence.

When several pledgets have been introduced it is a good plan to tie a knot in the string of the one to be withdrawn first, two knots in the second, and so on. Unless some distinction of this kind has been made the patient cannot know which string to draw first, and is as apt to make traction on the uppermost pledget as on the lowest.

In the vast majority of cases of peri-uterine trouble and inflammation of the appendages the nearest point of approach to it in the vagina is the part posterior to the cervix. The nearer the medication can be applied to the seat of the disease the more efficacious it will be. The logical deduction of these premises is that the medicated tamponade in the vast majority of cases should be placed behind the cervix, as shown in Fig. 4971.

In spasmodic and inflammatory conditions of the bladder, in acute ovaritis, or in tenderness of the uterine ligaments, the tamponade frequently affords relief by supporting and steadying the uterus, even when it is in normal posture. The most common application of the tamponade as a pessary is that made to retain the uterus in a normal position when first reduced from a retrodisplacement. The uterus, under these circumstances, is apt to be tender, and the surrounding tissues are too sensitive to tolerate a hard pessary. Indeed, where the circumstances will permit, a cure can be attained much more readily by persevering with the tamponade than by resorting to a pessary.

When the retroverted uterus is bound down by adhesions, the frequent applications of the glycerin tamponade, by its pressure and alterative action, will produce a stretching and absorption of the adhesions, and gradually allow replacement of the organ.

In partial or complete prolapse of the uterus a large astringent tamponade will often give more relief than any other support. If the vaginal and uterine supports are much relaxed, it may be necessary to retain the tamponade by a T-bandage. In rectocele and cystocele the tamponade is most serviceable. The astringent puckers up the vaginal walls, and ultimately restores their tone to a greater or less extent.

In 1878 Taliaferro, of Georgia, described a method of using the tamponade for the relief of subinvolution, areolar hyperplasia, descensus, and other dislocations of the uterus, with adhesions, chronic pelvic peritonitis, and cellulitis. His method simply introduced the element of pressure into the treatment already in use, thus stimulating circulation and hastening absorption in the same way that a snug roller bandage hastens the absorption of an exudation in the tissues of the leg. He places the patient in the knee-chest posture, and elevates the perineum with Sims' speculum. A few medicated pledgets are then packed into the fornix vaginæ with long dressing forceps, and upon them a solid column of tightly packed loose balls of wool or cotton is built, down to the floor of the pelvis. This column is flat antero-posteriorly, but reaches from side to side the full width of the vagina; or it may be varied in shape to make pressure where most desired.

Various methods have been devised by which the patient might be enabled to apply the tamponade herself. These methods are all to a greater or less degree deficient. Few women have sufficient dexterity and knowledge of the parts to enable them to apply a tamponade, in their own vaginæ, with any degree of efficiency, either through a special contrivance or a bivalve speculum. The idea is a delusion. If the tampon is to accomplish any beneficial results it must be applied carefully and intelligently, and with an eye single to the object to be accomplished in each individual case.

VIII. Vaginismus.—Vaginismus is a painful, involuntary, spasmodic contraction of the constrictor muscles of the vagina, firmly closing its canal and ostium. It may be due to structural changes in the hymen or the carunculæ myrtiformes, contact with which, or even the fear of contact, causing such violent contraction that coitus is precluded and even a digital examination becomes impossible unless the patient is anæsthetized. In such cases it is difficult to locate the source of the spasm. It is common in young, nervous, or hysterical women and is wont to declare itself at the first consummation of the marital rights; or it may develop during one of the following attempts at intercourse, being then due, in all probability, to the inflamed and sensitive state of the remnants of the hymen. It is produced sometimes by an irritable spot in the fossa navicularis, by urethral caruncles, by a vaginal or anal fissure, by the presence of an ulcer in the vagina, or by uterine or ovarian disease. Change of position in bed or washing of the genitals may cause an attack of vaginismus; it may also result from a lascivious dream, the patient awaking in pain from the spasm. In extreme cases convulsions and syncope may follow persistent attempts at coitus; and, on the other hand, nervous irritation with slight spasm may be induced by association with an impotent or partly impotent man.

In most cases the subjects of the disease are women who have been recently married, or women in whom, although perhaps married for several years, sexual intercourse has never been accomplished. In some instances, however, vaginismus first occurs after coitus has been enjoyed freely for months or even years, the symptom suddenly developing in consequence of an infection with gonorrhœa.

Sterility is almost the invariable result of vaginismus, and yet a few cases have been reported in which impregnation occurred without intromission.

In vaginismus superior—so called by Hildebrandt—the contraction occurs at some distance above the vaginal entrance, a sort of hour-glass contraction. In a few instances the contraction is voluntary; that is, the woman at will can prevent complete introduction of the penis, or, after it has entered, she can grasp and retain the or-

gan. Hildebrandt narrates the case of a woman in whom this power was developed to such a degree that she was able voluntarily to grasp the penis below the glans so firmly as to make its withdrawal impossible. The levator ani was the constricting muscle.

The diagnosis of vaginismus is not difficult. The labia majora and minora may be gently drawn apart, but the

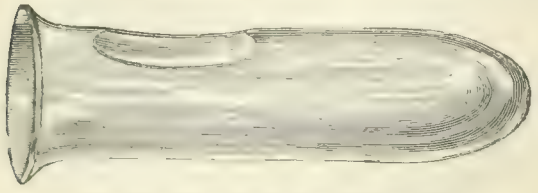

Fig. 4972.—Sims Glass Vaginal Dilator or Plug.

moment an effort is made to pass the finger into the vagina the pain, the spasm, and the wriggling of the patient may forbid any further examination without an anæsthetic. If the finger should overcome the resistance and find entrance, it may be so tightly grasped by the contracting muscles as to be benumbed. Frequently the patient is so hysterical that it is useless to make any attempt at an examination without the aid of an anæsthetic. As a rule, the anæsthesia must be very profound to permit of a thorough examination. In such cases it is best not to undertake the examination until arrangements have been made for operative interference, if such should prove to be necessary.

The treatment of vaginismus consists in absolute rest of the genital organs, all attempts at coitus being strictly forbidden. The hyperæsthesia of the parts may in some cases be relieved by hot sitz-baths or by applications of nitrate of silver (ten grains to the ounce), of a solution of chloral (four per cent.), or of carbolic acid (1 in 40). A four-per-cent. solution of cocaine is generally effective, but it must be used with caution. Ointments of belladonna or ichthyol sometimes afford relief. In fissure of the vagina or anus the base must be divided or touched with the thermo-cautery. Ulcers should receive appropriate attention, urethral caruncles removed, and irritable carunculæ myrtiformes snipped off. It may be necessary in some instances to excise the entire hymen and adjacent tissue. The edges of the wound thus made are then stitched with chromicized gut to secure primary union. As a matter of course an anæsthetic is necessary. In fissure of the neck of the bladder the urethra should be dilated to an extreme degree, the base of the fissure touched with a pencil of nitrate of silver or with the actual cautery, and a self-retaining catheter applied and left open for continuous drainage. In cases of obstinate spasm it becomes necessary to dilate the ostium vaginæ and its canal beyond the constrictor muscle. Such dilatation may be forcible and abrupt or gradual. The former is accomplished by introducing the thumbs into the vagina, the patient being anæsthetized, and separating the vaginal walls until the resistance is overcome by the rupture of some of the underlying structures, of which the most important is the sphincter vaginæ. Another method is to use a bivalve or trivalve or quadrivalve speculum as a dilator. The instrument is introduced closed into the vagina and then, after the blades have been opened, it is forcibly withdrawn.

Gradual dilatation without anæsthesia may be accomplished in many cases by means of the Sims glass plug or dilator (Fig. 4972). The parts are benumbed by the application of cocaine and the dilator is introduced. It is retained for an hour night and morning. The pain caused by its introduction soon ceases and may be mitigated by anointing the plug before introduction with a medicated ointment. The presence of the plug helps to obtund the sensibility. Day by day an instrument of larger size may be substituted until the vagina is overstretched.

When the dilator cannot be borne by the patient, an operation is the only recourse. With the patient anæsthetized the surgeon introduses two fingers of the left hand into the vagina and then firmly stretches the parts. With the scalpel he next makes an oblique incision about two inches long through the vaginal tissue on each side, extending from half an inch inside the ostium to the raphe of the perineum. More pressure is then made to distend further the vagina. Finally, the vagina is firmly packed with sterile gauze and a **T**-binder applied. Should there be little or no hemorrhage, the glass plug may be inserted at once; otherwise the gauze is left in place until the following day when it is removed and the glass dilator substituted. This instrument is then to be worn for a short time every day for several weeks, *i.e.*, during the healing of the wounds. The constitutional treatment, which should always accompany the local measures, consists in tonics of arsenic, strychnine, and glycero-phosphates, in outdoor exercise, and in change of scene. Complete sexual rest should be enjoined.

J. Riddle Goffe.

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VALERIAN.—(*Valeriana*, U. S. P.; *Valerianæ Radix*, B. P.; *Radix Valerianæ*, P. G.) The dried rhizome and roots of *Valeriana officinalis* L. (fam. *Valerianaceæ*).

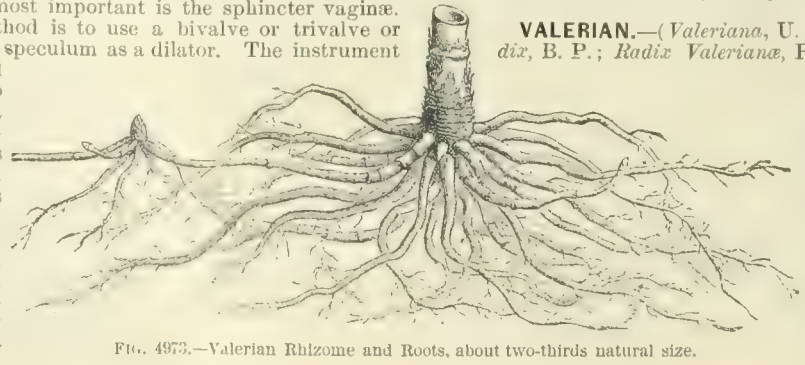

Fig. 4973.—Valerian Rhizome and Roots, about two-thirds natural size.

This perennial herb, native of the temperate parts of Europe and Asia, is a familiar object in our gardens, where it is grown partly as an ornament, partly for medicinal purposes. It is largely grown as

a drug in England, Holland, and other parts of Europe, though the product of wild plants is said to be superior. It should be collected and dried in the autumn. The rhizome is from 2 to 4 cm. (about 1 to 1.5 in.) long, and 1 to 2 cm. (about 0.5 to nearly 1 in.) thick, upright, subglobular or obconical, truncate at both ends, light-brown or yellowish-brown, internally whitish or pale-brownish, with a narrow circle of white wood under the thin bark; roots numerous, rather coarse, brittle, brown, with a thick bark and slender, ligneous cord; odor peculiar, becoming stronger and unpleasant on keeping; taste camphoraceous and somewhat bitter.

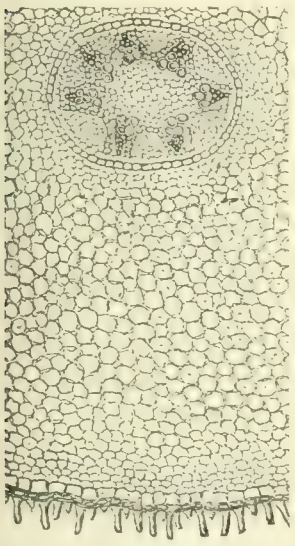

FIG. 4974. Cross Section of Valerian Root. (Baillon.)

Small, stunted rhizomes, grown upon dry, stony soil, are commonly superior to those of finer appearance.

The important constituents of valerian are: from one-half to two per cent. of volatile oil, and variable amounts of valerianic acid, of a camphor-like body very similar to borneol, and of resin. Both the volatile oil and the resin are mixtures, containing the camphor and valerianic acid. The oil consists chiefly of the terpene *valerin*. The proportion of these different substances varies greatly, according to the age of the drug after collection, the percentage of the oil thus usually decreasing, that of valerianic acid increasing.

Oil of valerian suitable for medical use is described in the Pharmacopœia as follows: "A greenish, or yellowish, thin liquid, becoming darker and thicker by age and exposure to air, having the characteristic odor of valerian, an aromatic, somewhat camphoraceous taste, and a slightly acid reaction. Specific gravity about 0.950. It is readily soluble in alcohol." Valerianic acid is also liquid, but thicker than the oil, colorless, of a strong valerian-like, but also sour and cheesy, odor, and a sour, burning taste. It is an active acid, forming salts with the metals and alkaloids, several of which are in use.

The intoxicating action of valerian on cats, which seem to have an irresistible craving for it, is well known. In very large doses, several drachms several times a day, it may produce, in man, dizziness, disturbance of vision, hallucinations, or active delirium. Nausea and vomiting are also likely to occur from such doses. It appears to be eliminated by the kidneys, which it stimulates slightly.

Its medicinal action is that of an antispasmodic, like musk, asafœtida, chamomile, lavender, etc., as well as ether and the bromides. Like most essential oils, it is also a general and digestive stimulant in moderate doses.

Valerian is frequently given to patients suffering from emotional unbalance, hysterical and "nervous" (in the popular sense) disturbances, headaches, and other pains due to the same causes, as well as wakefulness, with considerable benefit. It is also given in some more serious and obstinate diseases, as chorea or epilepsy, especially petit mal, with occasional benefit.

The most advantageous way of employing valerian is to give either one of the galenical preparations of the drug, or the oil.

The dose of the root is 1–2 gm. (gr. xv.–xxx.), of the official fluid extract an equal number of cubic centimetres or of minims. There is also an official tincture, strength one-fifth, and an ammoniated tincture, of the same strength in aromatic spirit of ammonia.

Henry H. Rusby.

VALERIANIC OR VALERIC ACID ($HC_5H_9O_2$).—Valerianic acid is the active constituent of valerian, whence it was first obtained for study. It is also the chief active constituent of cypripedium, and is found in various other aromatic drugs, such as angelica. Besides these natural sources, it is readily obtained by the chemical change of many organic substances, and is very largely manufactured by the oxidation of amylic alcohol with bichromate of potassium. Thus we have in the market a natural and an artificial acid. The natural acid is obtained by the distillation of valerian with water. The distillate is a mixture of volatile oil of valerian and valerianic acid, and a portion of the oil can be converted into the acid. This acid is divisible into the normal valeric and the isovaleric acids. The artificial acid produced from amylic alcohol is combined with sodium, from which it is then freed by sulphuric acid. This form is therefore more prone to impurity. If strictly pure, it is the practical equivalent of the natural acid. Valerianic acid occurs as a colorless, transparent, thin, oily, volatile, combustible liquid, with a strong odor, much like that of valerian, and an acrid, burning taste. It is soluble in both alcohol and water, the artificial pure iso-acid being much less soluble in water. The specific gravity of the pure natural acid is 0.940. Acetic acid has been used as an adulterant.

Valerianic acid shares the antispasmodic properties of oil of valerian, but is usually distinctly inferior to it. Its stimulating effect is spurious, it being distinctly weakening. It is capable of poisoning by cardiac and respiratory paralysis, the latter indicated by convulsions. It is used in hysteria and mania, in doses of three to ten minims. It is largely used for the administration of certain bases in the form of valerianates, and the valerianates of ammonium, quinine, iron, and zinc are official.

Henry H. Rusby.

VALERIDIN.—A synonym for sedatin (*q. v.*).

VALIDOL, menthol valerianate, a menthol ester of valerianic acid, is a clear oily liquid of mild aromatic odor and a not unpleasant cooling taste. It contains about thirty per cent. of menthol.

Neustatter gave the remedy in five cases of scintillating scotoma, with prompt disappearance of the flashing and the accompanying headache. Cipriani has employed it as an expectorant in bronchitis, as an anti-emetic in the vomiting of tuberculosis, and in pharyngeal or nasal catarrh as a spray or local application.

Goldmann recommends it in the treatment of nervous headache, migraine, neuralgia, and neurasthenia, and as a stimulating stomachic. Applied externally in hemicrania and such conditions, it exerts a sedative and analgesic action. Dose ten to thirty drops on sugar or in capsule.

W. A. Bastedo.

VANILLA.—U. S. P. (*Fructus Vanillæ*, P. G.) The fruit of *Vanilla planifolia* Andrews (fam. *Orchidaceæ*) peculiarly cured and dried.

The vanilla plant is an epiphytic climber, with fleshy stems and foliage, native of the forest regions of eastern Mexico. It is very extensively cultivated there, as well as in many parts of the Old-World tropics. As grown in these different regions it exhibits distinct varieties, and the products differ considerably in quality and in commercial value. The Mexican variety is still generally preferred in the United States, but the Bourbon article, as improved during recent years, is fast overtaking it in popular estimation.

Natural pollination of the flowers is so scanty that artificial pollination by hand labor is an important industry. Green vanilla fruits are very similar in appearance to green bananas, but relatively only about one-third as stout. They are gathered just when they begin to turn yellow. If left longer, they are apt to split at the

FIG. 4975.—Fruit of "split" Vanilla, one-fourth natural size.

ends in drying, which renders them less salable; though some good judges believe that these "splits," as they are commercially termed, are not inferior. The details of the curing process vary greatly in different countries, and even among different operators, but its essential features depend upon the fact that the odorous principle, vanillin, does not exist in the natural fruit and must be developed in the curing process. This usually consists of a sweating or steaming operation in a closed space, followed by alternating exposures in closed containers, or between woollen blankets. The "beans" thus treated gradually shrink in thickness and become darker until they assume the characteristic appearance described below. They are assorted into lengths, the more long and slender ones being preferred and selling higher. They are tied tightly into bundles, wrapped in paraffin paper, and packed in tight tin cans. Because of the loss in weight from over-drying, there is a temptation to underdry them, and many bundles, owing to this mistake, are found mouldy within, on being opened. The finest product is thus described: Bean-shaped fruits, from 20 to 25 cm. (8 to 10 in.) long and 5 to 8 mm. ($\frac{1}{3}$ to $\frac{1}{4}$ in.) thick, straight, except for the short-hooked base, flexible, longitudinally wrinkled, dark chocolate-brown, shining or covered with white crystals of vanillin, giving them a frosted appearance; one-celled, with three fleshy placentæ and innumerable minute seeds; having a strong, pleasant, and characteristic fragrance, and a sweetish, aromatic, and slightly fruity taste.

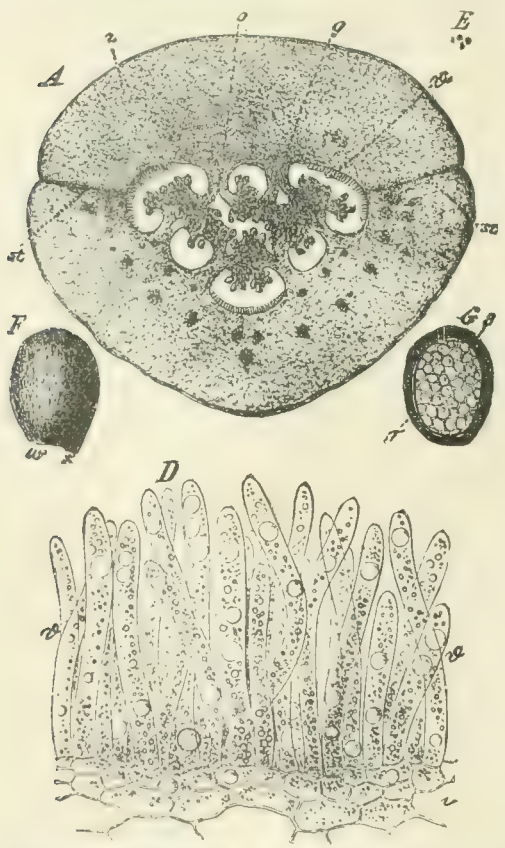

FIG. 4976.—A, Transverse section of Vanilla Pod, enlarged; E, seed, natural size; F, the same, magnified; G, section of same; D, the papillary gland hairs lining the cavity of the pod. (Berg.)

CONSTITUENTS.—The important constituent of vanilla, and that which represents its odor and taste, is from 1.5 to 2.5 per cent. of *vanillin*, *vanillic aldehyde*, or *methyl-protocatechuic aldehyde*, ($C_8H_8O_3$), which occurs in colorless prisms having the characteristic odor and taste of vanilla in intense degree; they melt at 80° to 81° C., and are soluble in alcohol, ether, and chloroform, and less so in water. With the vanillin, occur a little volatile and about ten per cent. of fixed oil, sugar, and other unimportant constituents.

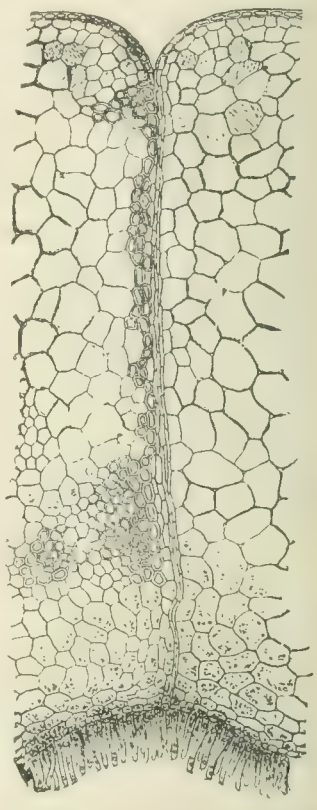

FIG. 4977.—Section of Vanilla through the Commissure where the Fruit splits. (Berg.)

SUBSTITUTES AND ADULTERANTS.—On account of the high price of vanilla and vanillin, both have been enormously substituted and adulterated. The use of inferior fruits of other species of vanilla, short, broad, flat, and of a strong fruity odor, must be classed as substitution. These usually cost only from one-tenth to one-twelfth as much as the best. The use of tonka beans and other substances containing cumarin is even more extensive. Finally, various compounds of prunes, raisins, and other substances are sold as vanilla substitutes. Cumarin is itself substituted for vanillin. Artificial vanillin is largely prepared from coniferin and eugenol, and, although apparently identical chemically with the natural, it has not been found equal to it in useful properties.

USES.—Vanilla has no active properties as a medicine, though the official ten-per-cent. tincture is sometimes used as an antispasmodic in fluidrachm doses. As an adjuvant for perfuming and flavoring, it has many uses in the pharmacy, as well as in confectionery and pastry.

Henry H. Rusby.

VANILLIN PARAPHENETIDIN, $C_6H_3.OH.OCH_3.CH.N.C_6H_4.OC_2H_5$ is formed by heating vanillin with paraphenetidin. It occurs in the form of crystals which are soluble in water, and in dose of 1 to 2 gm. (gr. xv.–xxx.) it has a hypnotic and antineuralgic action.

W. A. Bastedo.

VARIATION.—In its modern biological sense, *variation* is used to signify a difference or the presence of differences from some *type* taken as the standard of comparison. With a somewhat more limited meaning, the word *deviation* also is used as the name for a difference from the type of any organ or character. By *variability* is meant the extent of the deviations, together with the relative

number of individuals possessing each degrees of variation.

What Variation is Not.—Much confusion in regard to variation has arisen from the word having been employed loosely with meanings not in accord with the present usage. Therefore it may be well at the outset to call attention to the more important variations in the use of the word.

In the first place, it is necessary to distinguish between variation and *modification*. Following the suggestion of C. L. Morgan (1897), which has been adopted largely by biologists, we may employ the word *modification* as a technical term, to signify a change in any characteristic of an individual organism in response to some condition of its environment or the process by which such a change is brought about. Modifications were spoken of formerly as *acquired characters*, but the term *acquired* has frequently led to confusion in the minds of persons not perfectly familiar with the facts. It seems best, therefore, to abandon that term. A modification is a change produced in an individual. A variation is any difference in the individual from a certain ideal condition taken as the type. Thus a modification may produce or modify a variation, but modification and variation are two entirely distinct and independent concepts. An electric discharge may produce sound, but sound and electricity are not the same thing, and sound may be produced by other causes. Likewise, modification may produce variation, but they are not the same thing and variation may be due to other causes.

Theoretically we may follow Weismann in making a distinction between blastogenic and somatogenic variations; *blastogenic* variations being those due to differences in the constitution of the germs from which the group of individuals under consideration have developed, while *somatogenic* variations are differences which have arisen in the bodies (*somata*) of the individuals as the result of modification following exposure to different environmental conditions. But as has been pointed out by Vernon (1903), in the practical study of variation by statistical methods, it is generally impossible to make this distinction. This is due, in the first place, to the fact that blastogenic and somatogenic variations may be of the same kind and degree. Thus deafness may result from a pathological lesion, as in scarlet fever, or it may be due to a congenital malformation, which, owing to observed parental correlations, we must suppose to be of blastogenic origin. But even in such an extreme variation as this Fay (1898) found it impossible to determine in many cases to which class a given individual should be assigned. In the second place, every individual and even parts of individuals, are subject to constantly fluctuating environmental conditions from the moment of conception until death. These changes of surrounding conditions are met by corresponding responses, functional or structural, or both, on the part of the organism, but these reactions are themselves probably subject to variations independent of the exciting stimuli, and who can tell, therefore, how much of the similarities and differences in any group of organisms is due to similarities and differences in the structure of their germs, and how much to the various conditions of the environment to which they have been subjected? The importance of modifications in the normal development of organisms has been discussed in another article (see *Differentiation*).

The clearest examples of purely blastogenic variation are to be found in such mammalia as give birth to a considerable number of offspring at one time. For example, in a litter of puppies or kittens, all sired by the same male, all developed at the same time in the same uterus, we have a group of organisms where the conditions of parentage and environment are as uniform as possible, and yet variations in color, form, and mental traits will be readily apparent. These differences appear to be clearly blastogenic in origin, but the very general presence of a "runt" in such a litter indicates that the conditions of nutrition at least have not been quite uniform. Variation, then, as we understand the term at present, is not a broader term than modification, as Vernon (1903) would have it, but is an entirely distinct concept. Modification, on the other hand, may stand toward variation in the relation of cause to effect. Variations so effected are classed as somatogenic, as distinguished from blastogenic variations of purely germinal origin.

Moreover, our idea of variation does not include any change in the individual taking place during the course of its life, no matter whether that change be of blastogenic or somatogenic origin. Thus the changes which an individual insect undergoes in the course of its metamorphosis would not come within our definition of variation. But a group of insects, say the potato beetles in a certain field, would exhibit in each stage of their development variations from the type of that stage, and the degree of variability might differ in the successive stages.

Finally, the idea of variation does not necessarily include the parental relation. It is true that we may select one or the other parent, or both parents combined in an imaginary mid-parent (see *Heredity*) as the type, when dealing with the characters of offspring of identical or like parents. This is done in the study of heredity. But in the ordinary study of variation the investigator is usually ignorant of the parentage of his material. So a variation is not a difference from the parental type necessarily, but is a difference from any type that may be selected.

In fact, variation is a phenomenon by no means confined to organisms. It is shown as well by lifeless objects and events. Thus we may, if we choose, study the variability of the stones on the beach, of snow crystals, of the forms of clouds, of rainfall, of the height of the barometer, or of the price of wheat.

Aim and Method of Study.—Having now clearly in mind what is meant by variation, let us consider what it is that we may expect to gain by the study of this subject and the method to be pursued in such an investigation.

Every one who is at all familiar with modern theories of organic evolution knows that variation is of very great and very fundamental importance from the theoretical points of view. Variation is at the basis of every theory of evolution. Therefore, in order to understand evolution, we must know the facts of variation. (See *Evolution*.)

Variation is an important factor in the classification of animals and plants. Formerly the systematist simply took as the type of a species the individual that was first described. The modern methods enable him, when provided with sufficient material, to define the limits of a species with much greater accuracy and to select as the type a form that is truly representative.

To the physician the study of variation is of great importance. Every practitioner knows that the same disease may be manifested in diverse forms, and that patients vary in their reactions to treatment. A study of the types and variability of diseases and of the effects of treatment may be expected to add much toward a true appreciation of these subjects.

For the surgeon, variation is still more important. He must know what anomalies are likely to be met with and their relative frequency.

Variation has been studied extensively by teachers of gymnastics and the results have had practical application in the determination of the relative rank of the pupils and their degrees of improvement.

The method employed in the modern study of variation is statistical. This, as Pearson (1902*c*, p. 320) has well said, is "because the whole problem of evolution is a problem in vital statistics—a problem of longevity, of fertility, of health, and of disease, and it is as impossible for the evolutionist to proceed without statistics as it would be for the registrar-general to discuss the national mortality without an enumeration of the population, a classification of deaths, and a knowledge of statistical theory." This is true, not only for the problem of evolution, but also for all problems for which a solu-

tion may be sought in the phenomena of organic variation.

In order that this method may be employed, the data must be expressed in quantitative terms. We may no longer speak of things as being longer or shorter, heavier or lighter, but we must give the results of observations in exact units of length, weight, and the like. Or, if this be impossible, the observations must be divided into groups, so that each group shall be as nearly as may be equally divergent from the one on either side of it, in order that to each one may be assigned a serial number that can be used as a quantitative expression.

The statistical method for the study of variation was founded by Quetelet (1846), who showed that certain human characteristics follow in their relative frequency the mathematical law of the probability of error, which had been applied previously to astronomical and other physical observations. Darwin (1868) gathered a great many cases of variation, especially among domestic animals and plants, but he seems to have overlooked Quetelet, or, at any rate, he did not employ his method. The first attempt to study the variations of wild animals by exact quantitative measurements appears to have been made by J. A. Allen. But we are especially indebted to Galton (1889) for calling the attention of both socialogists and naturalists to the importance of the statistical method for the study of variation and heredity. He made considerable advances beyond Quetelet's use of the theory of probability, and his methods were quickly appreciated and used by persons interested in anthropometry. Weldon (1890) was the first to apply these methods in the study of variations of animals, and de Vries (1894) applied them in botany. He was quickly followed by Ludwig (1895), who had made previously extensive statistical investigations on plants (1883 *et seq.*).

While others had paved the way, naturalists are especially indebted to Pearson for his mathematical investigations beginning in 1893, which, it is safe to say, will be the foundation for all future work in statistical biology. Unfortunately, however, much of his writing is unavailable to any but those versed in the language of the higher mathematics. Dunker (1899) has done good service in giving an excellent elementary treatment of the subject as it stood at the end of the year 1898, and Davenport (1899) has furnished a useful manual of formulæ and tables. But both of these works are now (1903), in part at least, out of date, and a text-book that will enable the average naturalist or physician to understand and apply the principles laid down by Pearson is still very much to be desired.

Classification of Variations.—Before proceeding with the details of the statistical method it may be well to pause to consider the nature of the material to be studied.

In the first place it should be noted that every individual has many characteristics, and one of the limitations of the method is that it deals primarily, not with individuals as entire objects, but with single characters only. Part of this difficulty may be overcome in some cases by combining two or more characters in a ratio, usually called an *index*, as the *cephalic index*, the ratio of breadth to length of head, or the *strength-weight index*, which is the ratio of the sum of the strength tests to the weight. Such a ratio may then be treated like a single character.

Another difficulty that would be met with in an attempt to appreciate the variability of entire organisms arises from the fact that single characters in one individual differ greatly among themselves in the amount of their deviations from the values typical for the population as a whole. For example, it is very seldom that we meet with a man who has more or less than one nose, two eyes, a mouth, and the like; while, on the other hand, we find within certain limits all degrees of variability in stature, proportions of the face, color of the hair and eyes, and in various mental traits. So at the outset we may divide the characteristics of organisms into (1) those that are *normally stable* and (2) those that are *normally variable*. When a variation is observed in a character that is normally stable, it is so unusual an occurrence as to attract at once the attention of an observer familiar with the normal form. Gardeners call such variations "sports." Nectarines, our seedless fruits, double flowers, and many new varieties of flowers and fruits have arisen in the first place as sports. In animals polydactylism, albinism, and other monstrosities come within this class of unusual variations, which we may designate as *anomalies* in contradistinction to the *normal variations* of normally variable characters. Perhaps the normally variable characters may sometimes show variations that are so extraordinary as to be classed as anomalies, but it is hard to draw a line between these and the extremes of normal variation.

Bateson (1894) has divided variations into substantive, meristic, and homœotic. *Substantive* variations are differences in the substance of the organism, such as variations in size, weight, color, chemical composition, and the like. *Meristic* variations are differences in the number, division, and geometrical position of parts. *Homœosis*, or the occurrence of a homœotic variation, may be seen in a meristic series when a member of one series appears in the form characteristic of another series, as when in a flower one in the series of stamens appears in the form of a petal, or as when in a spinal column a vertebra of the lumbar series develops with the structure of a thoracic vertebra. In a case like the spinal column, however, where several series of structures are closely connected, it is not always possible to distinguish between homœosis and ordinary meristic variation.

It will be seen from this classification that variation opens a wide field for study. It would be useless to attempt to give illustrations of these classes in the present article, for every one will call to mind cases within his own experience, and to summarize the literature on the subject would require volumes. One wishing information in detail should consult Darwin's "Variation of Animals and Plants under Domestication" (1868), Bateson's "Materials for the Study of Variation" (1894), and especially Vernon's "Variation of Animals and Plants" (1903), which is an excellent summary of the results of recent investigations.

From another point of view variations may be classified according to their mode of occurrence into (1) variations between parts of an individual, (2) variations between individuals, and (3) variations between races or other groups of individuals.

In both animals and plants there may be produced in one individual a number of similar parts which show among themselves no differentiation connected in any marked degree with either their time of development, their relative position, or their relation to the environment (Pearson, 1902, p. 335). Such "undifferentiated-like organs" Pearson calls *homotypes*, and we may speak of the variation of such parts within a single individual as *homotypic variation*. Examples are variations in the number of veins in the leaves of a beech tree, the number of seeds in the pods of a pea vine, and the like.

If, instead of comparing similar characters of the same individual, we take like characters of different individuals, we may find what is called *individual variation*.* For example, we might count the number of ray flowers on the highest head of each one of a thousand plants in a field of daisies, or we might measure the stature of each man in a regiment of soldiers. Such observations would give us the data for the study of individual variations in these groups.

Finally, if a study of the data of individual variation shows that the observations tend to group themselves, not about a single type, but around two or more types (as determined by appropriate methods to be mentioned later), then each type may be taken as representation of a race or of a species, and we are confronted by the phenomena of *racial variation*. Under this heading would be included differences of type in the same locality as

* Pearson uses the term "individual variation" for what we have called homotypic variation and his racial variation is our individual variation. But our use of the latter term is more in accord with current American usage.

well as differences in different localities. In the first case the material would be said to be *heterogeneous;* in the second case, while it might be *homogeneous*, that is, variable about a single type, in each separate locality, it would likewise be heterogeneous as a whole. The heterogeneity of mixed material in the same locality is difficult to determine, but the presence of racial variability associated with difference of dwelling-place is a familiar phenomenon, especially to American ornithologists. Witness the races of Bob Whites, song sparrows, flichers, Western blue jays, etc. It is important to note the distinction between what we have called individual and racial variation, because a failure to do this leads to confused ideas as to the method of evolution.

Variation and Chance.—All human knowledge is an estimate of probabilities. But in the statistical study of variation the mathematical theory of probability, or doctrine of chance, is of especial importance, for it forms the foundation upon which the method is erected.

Most persons think of chance as something quite independent of law. They imagine an event occurring by chance as one quite impossible of prediction, and the Darwinian theory has been criticised because it supposes race progress to depend upon the survival of "mere chance variations." On the contrary, while it is perfectly true that we are frequently unable to predict single events, it may be shown, nevertheless, that chance follows very definite laws, which may be expressed by exact mathematical formulæ.

In order that the discussion of statistical methods may be clear, it is necessary to call to mind at this point those principles of probability that especially concern our subject.

In the first place, "the theory of chance consists in reducing all the events of the same kind to a certain number of cases equally *possible*, that is to say, to such as we may be equally undecided about in regard to their existence, and in determining the number of cases *favorable* to the event whose probability is sought. The ratio of this number to that of all the cases possible is the measure of this probability, which is thus simply a fraction whose numerator is the number of favorable cases, and whose denominator is the number of all the cases possible" (Laplace, 1902, p. 6).

This definition of probability, which is the first principle of Laplace (*loc. cit.*, p. 11), may be illustrated by the tossing of a coin. Suppose I drop a silver quarter upon the table: it may come to rest either with the goddess of liberty or with the eagle on the upper side, "heads or tails." We have, then, two equally possible events resulting from the tossing of the coin. Suppose A bets that the throw will be heads, and B takes him up. There are two possible events, of which one is favorable to A, so the probability of his winning is expressed by the ratio one-half, but the other one of the two possible events is favorable to B, and the probability of his winning is also expressed by the ratio one-half. The probabilities for and against heads being the same, the bets on the game should be even. All the equally possible events that may produce or prevent a result are called the *chances* of that result (Quetelet, p. 10). The chances may be favorable or unfavorable; if all favorable, the result is a certainty. It will be noticed that the probabilities for and against the event added together equal unity, which is the mathematical expression for certainty. Thus in mathematics the various degrees of probability are expressed by fractions which may have any value between 0 and 1. It should be noted also that the probability of a given result remains the same no matter how many possible events may affect it, provided that the ratio of favorable events to total events remains the same. Suppose, for example, that A and B play with dice instead of a coin. A cube has six faces, any one of which may rest uppermost. Let A bet that the upper face will show more than three spots, he wins if it shows four, five, or six; that is, there are three favorable out of six possible chances, and the probability of his winning is $\frac{3}{6} = \frac{1}{2}$, as before. But suppose that he wagers on the throw being an ace, then he will lose if any one of the other five sides turns up. His probability of success is then $\frac{1}{6}$, and the probability of the stakes going to B is $\frac{5}{6}$. In making the bets, therefore, B should give odds to A of five to one. What this means is, that, while we cannot predict the result of a single throw of coin or dice (for if we could the probability would be certainty), this calculation enables us to foresee that in the game of heads and tails or in throwing dice for more than three spots, the number of successes will in the long run equal the failures, or in the throwing of aces will be in the proportion of one to five, provided always that the coin or dice are perfectly symmetrical in form and weight.

The closeness of observation to theory is illustrated by an experiment made by Quetelet (*loc. cit.*, p. 93). He placed in an urn 40 white and 40 black balls, and then drew one ball at a time, which was replaced after its color had been recorded. He made in all 4,096 drawings, and according to the theory of probability the result should have been 2,048 white balls and the same number of black. The actual results were 2,066 white and 2,030 black balls, an error of only $\frac{8}{1000}$.

The theory of probability teaches us how to judge of future events by past experience; it is thus common sense reduced to mathematical expression. Suppose, as does Quetelet (*l.c.*, p. 14), that we wish to determine the probability of drawing a white ball from an urn. We upset the urn and count the balls. If we find two white balls, three red, and four black, we answer that the probability of drawing a white ball at the first draw, the balls having been replaced, will be $\frac{2}{9}$.

But let it be impossible to upset or to see into the urn, and let only one ball be drawn at a time, which must be replaced before drawing another. Having no previous knowledge of the contents of the urn, we may suppose it to contain any number of balls of any color mixed in any proportion. The probability of drawing a white ball at the first draw may have any value from 1 to 0. We may suppose this value to be $\frac{1}{2}$. We draw a ball which is white, and it is then replaced. Now we know that the urn contains one white ball, and we may guess as before that the rest of the balls are in equal proportions of white and colored. There would then be on this hypothesis two chances of drawing a white ball to a total of three chances, and the probability would be $\frac{1+1}{1+2} = \frac{2}{3}$. A second draw is made with the same result. Now we know that the urn contains two white balls, and the probability that the third ball will be white becomes $\frac{2+1}{2+2} = \frac{3}{4}$. Similarly after ten white balls have been drawn in succession, the probability that the next ball will be white is $\frac{10+1}{10+2} = \frac{11}{12}$, and after ninety-eight repetitions of this result it is increased to $\frac{98+1}{98+2} = \frac{99}{100}$ (Quetelet, *l.c.*, p. 367). This is but a rough illustration of a principle that mathematicians arrive at by a somewhat different line of reasoning involving the processes of the integral calculus. The rule is: "That an event having occurred successively any number of times, the probability that it will happen again the next time is equal to this number increased by unity and divided by the same number increased by two units" (Laplace, p. 19).

Thus from the analogy of the urn we see how we may judge of the probability of future events in nature. If, for example, I examine one hundred specimens of a certain kind of animal and find that each one has six legs, the probability that the next one examined will have six legs is $\frac{101}{102}$, a value so near unity that I may safely infer that the number of legs in this species is a normally stable character. Putting the extent of historical time at 5,000 years, or 1,826,213 days, during which time the sun is known to have risen regularly during every twenty-four hours, the probability, aside from all other considerations, that it will rise to-morrow is $\frac{1,826,214}{1,826,215}$,

or the chances that it will not rise are about one in two million. Thus we see how the factor of doubt in regard to any deduction decreases with the increase in the number of observations upon which the deduction is based. Whatever may be the true value of this unknown factor we may reduce its relative value to any extent we please by continuing the observations to any desired limit. An explorer who upon entering an unknown island should meet two men, both black, would still have considerable doubt as to the color of the rest of the inhabitants. But after he had seen a thousand of the natives and found them all black, he would be justified in thinking that to be the color of the whole population.

Another principle similar to the preceding may be illustrated by returning again to the urn. Suppose that the result of the first nine consecutive drawings was five white and four black balls, the probability of drawing a white ball next time would be expressed by $\frac{5+1}{5+4+2}=\frac{6}{11}$; and if the result of ninety-nine drawings was fifty-five white and forty-four black balls the probability that the hundredth ball will be white is $\frac{55+1}{55+44+2}=\frac{56}{101}$. Thus in such cases in which observations show two possible results, the probability that one of these results will occur again is expressed by a fraction whose numerator is the number of times that result has been observed plus one, and whose denominator is the total number of observations plus two (Quetelet, p. 27). Here, again, we see the factor of doubt decreasing in relative value with the increase of the number of observations, so that, if after a large number of drawings we still get the same relative numbers, we may conclude that the urn contains only black and white balls, and that the proportion of white to black is five to four. Hence with a sufficient number of observations the factor of doubt practically vanishes and we may consider the chances favorable to each of the results to be in the same proportion to the total number of chances that the number of times each result has been observed is to the total number of observations (Quetelet, p. 29). When there are several possible results the calculation is rather complicated, but this rule practically holds good.

This principle is applied in calculating the proportion of the sexes. Thus Quetelet, taking the data from all the rural districts of Belgium during the year 1841, found that there had been born 53,437 male children and 49,788 females, giving a proportion of 1,072 males to 1,000 females. But taking the data for nine years, 1834 to 1842, he found the proportion to be 1,063 to 1,000, which is the same as the result obtained later by Oesterlen from the records of 59,350,000 births gathered from several countries of Europe. (See article *Sex*.)

One of the most important of the principles of probability is that, "If the events are independent of one another, the probability of their combined existence is the product of their respective probabilities." (Third principle of Laplace, *l.c.*, p. 12.) For example, if A toss a coin, the probability of heads is one-half; likewise the probability of B's coin giving heads is one-half. If A and B toss their coins at the same time, there are four possible combinations, but in only one of these do both get heads, thus:

	(1)	(2)	(3)	(4)
A—heads	heads	tails	tails
B—heads	tails	heads	tails

So the probability that both A and B will throw heads (1) at the same time is $\frac{1}{4}$, which is equal to the product of the probabilities that A and B will throw heads, respectively, multiplied together, $\frac{1}{2}\times\frac{1}{2}=\frac{1}{4}$. For the same reason the probability that both will throw tails (4) at one time is $\frac{1}{4}$, and $\frac{1}{4}$ is likewise the probability that A will throw heads at the same time that B throws tails (2), and that B throws tails when A throws heads (3). But combinations (2) and (3) give like results, namely, heads and tails. So there are two chances of heads and tails against two that the throws will be either both heads or both tails, and the probability is $\frac{1}{2}$. Thus heads and tails thrown with two coins is a complex combination, and its probability is the sum of the probabilities of the two simple combinations of which it is composed, $\frac{1}{4}+\frac{1}{4}=\frac{1}{2}$. It may be noticed that these values, $\frac{1}{4}$, $\frac{1}{2}$, $\frac{1}{4}$, are the terms of the expanded binomial $(\frac{1}{2}+\frac{1}{2})^2$.

If C comes into the game the number of possible combinations is increased as follows:

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
A—h	h	h	t	t	h	t	t
B—h	h	t	h	t	t	h	t
C—h	t	h	h	h	t	t	t

The number of possible combinations is now $8=(2)^3$, and of these only one favors the throwing of heads by all three players, the probability of that result being, therefore, $\frac{1}{8}=(\frac{1}{2})^3$. But there are three combinations, giving two heads to one tail. The probability of each of these is $\frac{1}{8}$ and the sum of the probabilities is $\frac{3}{8}=3\times\frac{1}{2}\times(\frac{1}{2})^2$. The probability of two tails and one head is also $\frac{3}{8}$, and of all tails is $\frac{1}{8}$. Again we have a series, $\frac{1}{8}$, $\frac{3}{8}$, $\frac{3}{8}$, $\frac{1}{8}$, which forms the terms of an expanded binomial, $(\frac{1}{2}+\frac{1}{2})^3$.

Now putting these figures into more general terms, we may represent the probability that a single throw will be heads by p, and that it will be tails by q. Let n equal the number of coins used and N the number of throws of the n coins together. Then the *frequency* of each combination of heads and tails will be represented by the terms of the binomial $N(p+q)^n$ when expanded. But in order that all the terms may be whole numbers, N must at least be equal to 2^n (greater when p and q are not equal), and the number of terms will be $n+1$.

With the view of illustrating the truth of this formula Weldon (1898) made four series of 4,096 throws of 12 dice ($4{,}096=2^{12}$), and counted the number in each throw of dice that showed more than 3 spots. The results are as follows:

Number of dice with more than three spots.	Terms of $4096(\frac{1}{2}+\frac{1}{2})^{12}$.	Observed Frequencies.			
		i.	ii.	iii.	iv.
12	1	0	1	0	1
11	12	11	13	8	14
10	66	71	86	61	66
9	220	257	246	241	241
8	495	536	540	513	586
7	792	847	836	856	861
6	924	948	913	948	866
5	792	731	750	802	728
4	495	430	446	420	474
3	220	198	198	182	204
2	66	60	55	51	67
1	12	7	12	13	6
0	1	0	0	1	0

The closeness of observation to theory is more clearly apparent in the diagram (Fig. 4978). The solid line is a polygon of thirteen points, the abscissa and ordinate of each point being proportional, respectively, to a number from the first column and the corresponding number on the same line in the second column of the table. The other polygons are formed in the same way, but with ordinates taken from the columns of observed frequencies. The first polygon is a graphic representation of the result expected on the theory of probability, supposing the dice to be perfectly symmetrical.

It will be noticed that the observed polygons lean slightly toward the side of the greater number of spots. This is readily explained when it is noticed that the dice are slightly excavated at each spot, and the side with six spots is opposite the ace. There is therefore a slight eccentricity of the centre of gravity, which tends to cause the greater number of spots to turn upward. These facts serve as a simple illustration of the way in which the study of probabilities may lead to the discovery of previously unknown causes of observed facts. Thus we see that in this case, in order to make our formula exact-

ly represent the facts, p should be made slightly greater than q.

This is illustrated further in another series of 4,096 throws of 12 dice, in which Weldon counted the number

When the chances for and against the event to be observed are even, when $p = q$, the curve will be symmetrical about the middle point, which is the highest. When the chances are uneven, when p is greater or

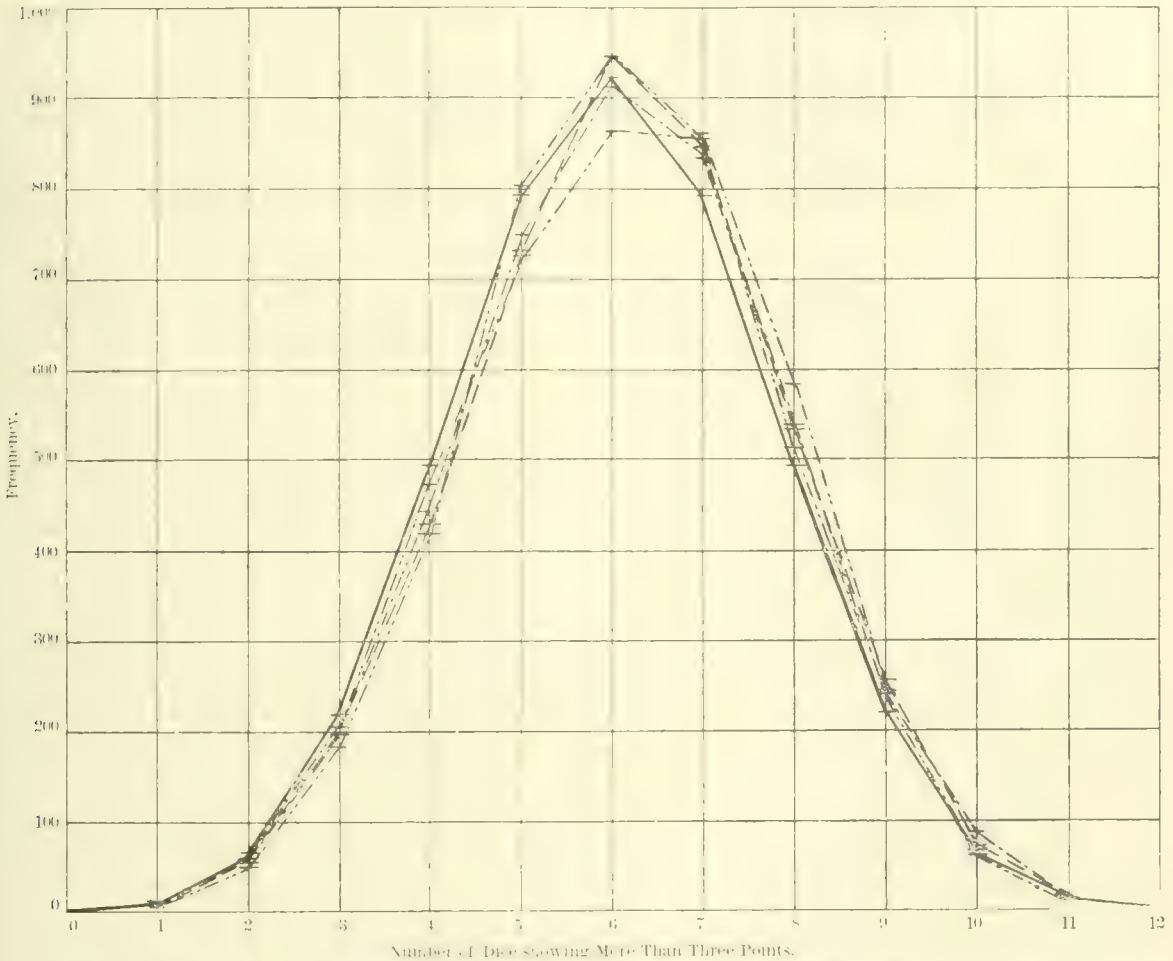

FIG. 4978.—Binominal Curve of Probability, terms of $4{,}096\ (\frac{1}{2} + \frac{1}{2})^{12}$, compared with the frequencies of the numbers of dice showing more than three points, in each of four series of trials with twelve dice, the number of throws in each series being $2^{12} = 4{,}096$. Binominal curve; ——, observations series I — — —, II — . — . —, III — . . — . . —, IV — — . . — — . . — —.

of sixes. Each die having six faces, the probability that one of them will turn up is $\frac{1}{6}$, and that it will not is $\frac{5}{6}$. So in this case $p = \frac{1}{6}$ and $q = \frac{5}{6}$. Thus our formula becomes $4{,}096\ (\frac{1}{6} + \frac{5}{6})^{12}$.

The calculated and observed results are as follows:

Number of sixes.	Terms of $4096\ (\frac{1}{6} + \frac{5}{6})^{12}$.	Observed frequencies.
8	0.58	1
7	4.66	7
6	27.18	24
5	116.43	115
4	363.84	389
3	808.53	796
2	1,211.44	1,181
1	1,102.56	1,145
0	459.52	447

The graphic representation of these results in Fig. 4979 is strikingly different from the curves in Fig. 4978. The latter were symmetrical or nearly so, while in the former both curves are distinctly asymmetrical, or *skew*. Thus we have two types of curves, or polygons, of frequency.

less than q, the curve will be skew, and the *skewness* will be greater the greater the difference between p and q.

When we abandon games of chance and seek to apply these formulæ to the study of physical and biological phenomena, the problem is reversed. The measurements made and their "observed frequencies," whose sum $= N$, are our facts, and p, q, and n become unknown quantities. For example, a man's stature depends upon n factors, such as food, climate, ancestry, etc., and p and q are the probabilities for or against an increase or diminution of stature as the result of each of them. The problem of finding a mathematical curve that will fit the facts now becomes too complex to be solved by the binomial theorem and requires formulæ derived by means of the calculus, but which may be used, nevertheless, with the aid of proper tables, by persons not familiar with that important branch of mathematics. When variations are distributed symmetrically on both sides of the type, the curve may be found by the "method of least squares," which was employed originally to determine the range of error in astronomical observations. But when the distribution is skew, Pearson (1902) has shown that it is

better to use the "method of moments," borrowed from the science of mechanics.

Collection and Tabulation of the Data.—The object of the statistical method for the study of variation is to represent in intelligible form the facts as they occur in nature. It is of the greatest importance, therefore, that the facts should not be obscured by any personal bias in the collection of the data. The data must be collected methodically at random.

Sometimes, however, the forces of nature themselves may tend to falsify the results and must be guarded against. For example, if we wish to determine the variability of shells due to the factors affecting growth, we must be sure that the proportions of the shell have not been affected by the erosive action of chemical substances or of parasitic algæ.

Finally, the data may not give true results if the observations are not sufficiently numerous. We must have a fair sample of the population. It has been seen in the case of the dice, that with 12 independent factors we cannot expect to get all the possible combinations in less than 4,096 observations. In practice it is found that usually 1,000 observations give sufficiently close results; 2,000 would be better, but sometimes 500 will do.

For statistical purposes we may divide normal variations into two classes: (1) *discrete* variations, in which the differences between individuals are sharply defined; and (2) *conjacent* (L. *conjacere*, to lie together) variations,

FIG. 4979. Binomial Curve of Probability, terms of $4,096(\frac{1}{6}+\frac{5}{6})^{12}$, compared with the frequencies of the numbers of sixes thrown in a series of trials with twelve dice, the number of throws being $2^{12} = 4,096$. Binomial ——, dice — — —.

in which the smallness of the differences that may be observed is limited only by the precision of our instruments.

Discrete variations are usually observed by counting, as the number of ribs on a shell, the number of ray flowers on a daisy, or of veins in a leaf. Most meristic variations would be in this class.

Observations of conjacent variations are usually obtained by measuring or weighing—as stature (Fig. 4980), strength of pull, and the like. In this class would come the indexes obtained by taking the ratios of two or more measurements. It would include also qualities not quantitatively measurable, like the color of the eye or ability in mathematics. The method of assigning quantitative values to such qualities has been alluded to in a previous paragraph. Thus most of the substantive variations would fall within this class.

The measurements having been made and recorded, the next step is to arrange the data in a table so as to show the number of times each value has been observed. An example will make this clear. Davenport (1900) counted the number of grooves on the inside of 1,046 scallop shells (*Pecten irradians* Lamarck, right-hand valve). His results may be tabulated as follows:

VARIATION IN THE NUMBER OF GROOVES ON THE SHELLS OF PECTEN IRRADIANS.

Classes	1	2	3	4	5	6	7	8
Values	14	15	16	17	18	19	20	21
Frequencies	2	15	108	515	308	90	7	1

That is, there were 2 shells with 14 grooves, 15 had 15 grooves, 108 had 16, and so on up to 21 grooves, which were found in only 1 shell. Each group of shells having a certain number of grooves forms a *class*, the number of grooves possessed by individuals of each class is its *value*, or magnitude, and the number of individuals in each class is its *frequency*. The classes may be numbered consecutively, and in some of the calculations to follow the arithmetic may be simplified by using these serial numbers in place of the values.

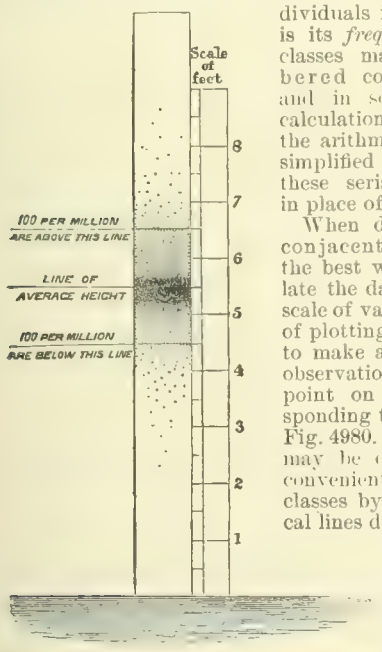

FIG. 4980.—An Example of Conjacent Variation. A supposed record of the statures of a large number of men. (From Galton.)

When dealing with conjacent variations the best way to tabulate the data is to lay off a scale of values upon a sheet of plotting paper, and then to make a mark for each observation opposite the point on the scale corresponding to its value, as in Fig. 4980. Then the marks may be divided into any convenient number of classes by a series of vertical lines drawn from points equal distances apart upon the scale. The number of marks between each pair of lines will be the frequency of the class. For example, De Vries gives the results of measuring the length of four hundred and forty-eight common red spotted beans (*Phaseolus vulgaris*), which may be tabulated in the following manner:

VARIATIONS IN LENGTHS OF BEANS OF PHASEOLUS VULGARIS.

Classes	1	2	3	4	5	6	7	8	9
Mid-values, mm.	8	9	10	11	12	13	14	15	16
Frequencies	1	2	23	108	166	106	33	7	1

In this case all specimens shorter than 8.5 mm. would go in class 1, those between 8.5 mm. and 9.5 mm. go in class 2, those between 9.5 mm. and 10.5 mm. in class 3, etc. These values, 8.5, 9.5, 10.5, . . . etc., mm. may be called the *class limits*.

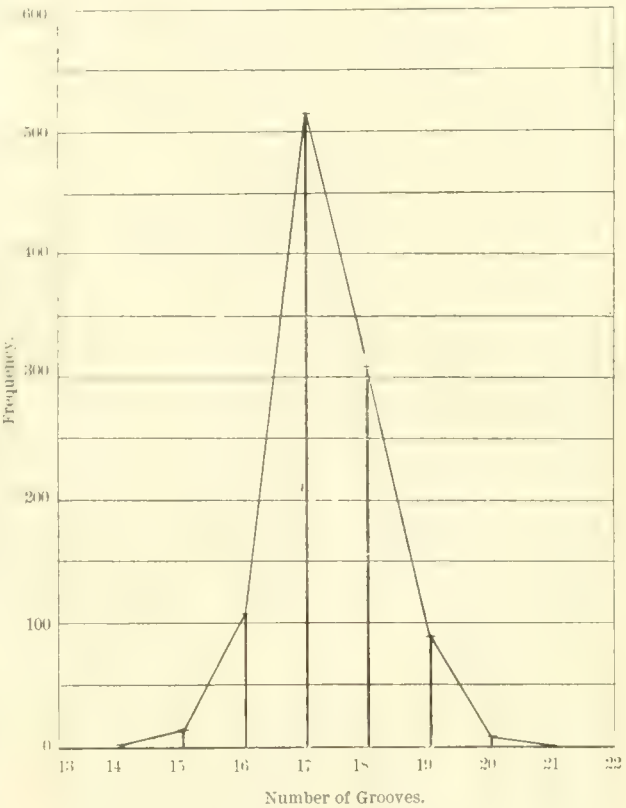

FIG. 4981.—Polygon of Frequency: Grooves on inside of scallop shells. (Data from Davenport.)

The results of these tabulations may be represented to the eye by polygons of frequency similar to those used to illustrate the results of throwing dice. Using plotting paper ruled in squares, we lay off a horizontal scale of values and a vertical scale of frequencies. Then the method of procedure differs according to whether we are dealing with discrete or with conjacent variations. In the case of discrete variations, the value of each class is taken as an abscissa from an imaginary zero point on the left and the corresponding ordinate is raised from zero at the base line to a point on the vertical scale corresponding to its frequency. Then connecting the tops of the ordinates by straight lines gives the polygon of frequency (Fig. 4981).

In the case of conjacent variations where there are many classes, the polygon may be constructed in a similar manner by taking the mid-values as abscissæ for the ordinates. But a more exact method, especially when there are few classes, is to construct the polygon of a series of rectangles, as in Fig. 4982, where the sides of the rectangles have for abscissæ the limiting values of the classes, and their heights are proportional to the corresponding frequencies.

A comparison of Figs. 4981 and 4982 with Figs. 4978 and 4979 show striking resemblances and suggests at once

that these variations in shells and beans follow the same general laws of chance that are found in the throwing of dice. This inference is confirmed by the results of a large number of studies of organic variation.

In a case of discrete variation the division of the data into classes presents no difficulties, but with conjacent variations the division is purely arbitrary, and here the theory of probability comes in as an aid to one's judgment. The following table, extracted from one given by Quetelet (1846, p. 90) shows how many observations are required in order that the data may be expected to fall symmetrically into certain numbers of classes. It is based upon the properties of the binomial $N(p+q)^n$ when $p = q$.

Number of observations.	Number of classes.	Number of observations.	Number of classes.
4	3	256	9
8	4	512	10
16	5	1,024	11
32	6	2,048	12
64	7	4,096	13
128	8	8,192	14

It will be noticed that for each additional class the number of observations needs to be doubled.

Discovery of the Type.—The data having been arranged as indicated in the preceding section, we are prepared to determine the type, or typical value, from which the variability of the character in question is to be measured. Referring to Figs. 4981 and 4982, we see in each case that there is a class which has a greater frequency than the others, and from its midordinate the polygon slopes away at first rapidly and then more gradually to zero on each side. The most obvious type would be the value of this class of maximum frequency. But experience and theory show that this would not be a very exact standard, unless our sample comprised a very large proportion of the total population. This is especially true of conjacent variations on account of the artificial character of the class boundaries. For example, in our case of the beans the class of maximum frequency has a medium length of 12 mm. But suppose the classes had been arranged so that the midordinates would fall at 8.5, 9.5, 10.5, etc., mm.; then the maximum frequency might have been found at either 11.5 or 12.5 mm. There is, however, a corresponding type called the *mode*, which is measured by the position of the ordinate of maximum frequency of the *theoretical curve* corresponding to the observed polygon of frequency (Pearson, 1896, p. 345). But the exact calculation of the mode, which is of considerable theoretical importance, involves a rather extended mathematical operation. A less exact, but very easy method will be described later.

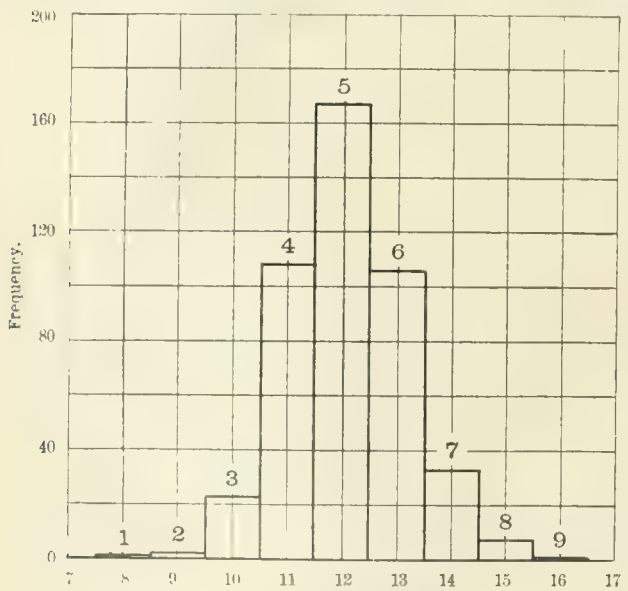

FIG. 4982.—Polygon of Frequency: Lengths of red-spotted beans. The serial numbers of the classes are placed above the corresponding rectangles. (Data from de Vries.)

The type usually employed is the average, or arithmetical mean, commonly called the *mean*. This may be discovered by adding all the observations together and dividing the sum by their number. But in order to avoid this long addition, the usual method is to multiply the value of each class by its frequency, add the products, and divide the sum by the number of observations. This operation is represented by the formula $M = \frac{\Sigma(Vz)}{N}$ where M = mean, V = values, z = frequency, N = number of observations, and Σ is the sign for summation. The same result may be obtained by taking the serial numbers of the classes for the values of V, and, having obtained the value of M in these units, it is easy to substitute the corresponding value in terms of the units of measurement employed in making the observations.

A third type, of considerable importance in certain cases, is called the *median*. This is the middle value, the value above which and below which fifty per cent. of the cases fall. It is easily found by simply counting off half of the observations arranged in order of magnitude. For example, if we have measured four hundred and fifty-one beans and arranged them in the order of their lengths, then the median will be the length of the two hundred and twenty-sixth bean, counting from either end of the series. If there are four hundred and fifty beans, an even number, the median will be intermediate between the length of the two hundred and twenty-fifth and the two hundred and twenty-sixth bean.

The same result may be obtained by a simple geometrical construction. Having for convenience reduced the frequencies to percentages of the total number of observations, the frequency of class 2 is added to that of class 1, to the sum of these class 3 is added, to this sum add class 4, and so on for all the classes, as in the following table. Thus we get a series of "sums from the beginning," which may be plotted as in Fig. 4983, using the method employed in the construction of Fig. 4982. Comparing the two figures, both made from De Vries's measurements of beans, we see that the first rectangle in the two is the same, the second in Fig. 4983 is composed of 1 and 2 in Fig. 4982, the third, of 1, 2, and 3, and so on until the ninth column in Fig. 4983 has the same area as the sum of all the nine rectangles in Fig. 4982. Now, drawing a diagonal from the lower left-hand to the upper right-hand corner of the upper rectangle in each one of the columns of Fig. 4983, we obtain what is called a *polygon of distribution*. It shows the distribution of the variations in our sample of the population. Turning the diagram around so that the scale of frequencies is horizontal, we see that the outline of this polygon is of the same general form as a line that might be drawn so as to touch the tops of the beans if they were stood up side by side in the order of their lengths. First there would be two or three very short beans, then a little row of beans 9.5–10.5 mm. high, then a much longer row, 10.5–11.5 mm. high, etc. Now, with the diagram in its first position, draw a horizontal line from the fifty-per-cent. point on the scale of frequencies to the middle rectangle, cutting the side ac at d and the diagonal, cb at m. Then draw a vertical line from m, and at its point of intersection with the scale of measurements read off the value of the media[illegible] To insure ac-

DATA USED IN CONSTRUCTION OF POLYGON OF DISTRIBUTION (FIG. 4983).

Class numbers.	Mid-values mm.	Frequency.	Per cent.	Sums from beginning per cent.
1	8	1	0.2	0.2
2	9	2	0.4	0.6
3	10	23	5.2	5.8
4	11	108	24.1	29.9
5	12	167	37.2	67.1
6	13	106	23.7	90.8
7	14	33	7.4	98.2
8	15	7	1.6	99.8
9	16	1	0.2	100.0
	....	448	100.0	

curacy, the diagram should be made on a large scale and be drawn with great care. A better way is to calculate the result numerically. Turning to the diagram, it is evident that the triangles *acb* and *dcm* are similar. Hence $dm : ab :: cd : ca$ and therefore $dm = ab \cdot \frac{cd}{ca}$.

Let N be the total number of observations. Then we have the rule: Multiply the range of the middle class (ab) by $\frac{1}{2}N$ minus the sum of the frequencies of all the lower classes ($= cd$), divide by the frequency of the class (ca) and add the magnitude of the lower limit of its range. The result will be the median magnitude. In our example of the beans, $cd = 50 - 29.9 = 20.1$ per cent.; $ab = 1$ mm.; and $ca = 37.2$ per cent. Hence $dm = 1 \times \frac{20.1}{37.2} = 0.54$ mm.

The lower limit of class 5 is at 11.5 mm. Therefore the median is $11.5 + 0.54 = 12.04$ mm. This method assumes, of course, that the values in the middle class are evenly distributed.

In the same manner may be determined the value of the measurement corresponding to any other point on the scale of frequencies, as at ten per cent., twenty per cent., etc. These values are called *percentile grades* (Galton, 1889), and they have been used extensively for the study of variations of anthrometric measurements; especially by teachers of gymnastics, who use these grades as a means of determining the standing of their pupils before and after training.

We may derive, then, from each collection of data three values, the mean, the mode, and the median, each one of which may serve as a type from which to measure variability. When the deviations from the mean are distributed symmetrically on both sides of it, all three of these values are the same. But they differ when the distribution is skew, as in throwing sixes with dice and in most variations found in nature. In such cases the median always lies between the mean and the mode, and the deviation of the median from the mean is one-third the deviation of the mode. This rule provides an easy way of calculating the *mode*, which, according to Pearson (1902, p. 261), is quite good enough for practical purposes in most cases, and avoids the tedious mathematics of the more exact method. (Compare *a*,*c*, and *b* in curves of Type III, Fig. 4986.)

The Measure of Variability.—Taking the mean as the type of any given character or organ, the problem is now to find a quantitative expression for the variability of that character in the group of organisms under observation. The first step is to calculate the deviation (x) of each class from the mean (M) by subtracting the values (V) of the classes from the mean. In the case of the beans, the mean is 12.05 mm. Omitting the small fraction for the sake of simplicity, the deviations of the several classes are given in the fourth column of the following table.

Now if the deviation of each class be multiplied by its frequency (z), the results added without regard to signs, and the sum divided by the number of observations, we

CALCULATION OF THE VARIABILITY IN LENGTH OF RED BEANS, PHASEOLUS VULGARIS (DATA FROM DE VRIES).

Classes.	V.	z.	x.	xz.	x^2z.
1	8	1	−4	−4	16
2	9	2	−3	−6	18
3	10	23	−2	−46	92
4	11	108	−1	−108	108
5	12	167	0	0	0
6	13	106	1	106	106
7	14	33	2	66	132
8	15	7	3	21	63
9	16	1	4	4	16
				$\Sigma(xz) = 361$	$\Sigma(x^2z) = 551$

$N = 448$

$M = 12$ mm. $A\,D = \frac{\Sigma(xz)}{N} = 0.8023$ mm.

$\sigma = \sqrt{\frac{\Sigma(x^2z)}{N}} = 1.1065$ mm.

obtain the *average deviation*. This is represented by the formula $A\,D = \frac{\Sigma(xz)}{N}$ and is one measure of variability. But it is rarely used.

The measure of variability most frequently employed at present is what is called the *standard deviation*. This is the square root of the average of the squares of the deviations, and is represented by the symbol σ, as in the formula: $\sigma = \sqrt{\frac{\Sigma(x^2z)}{N}}$

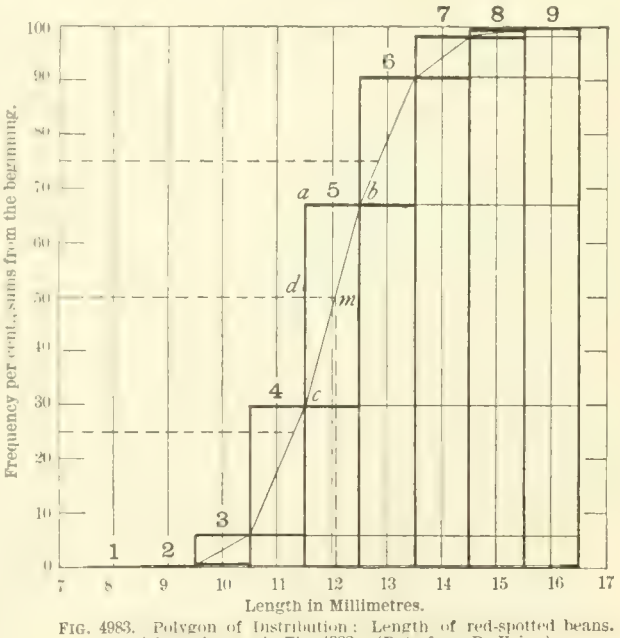

FIG. 4983. Polygon of Distribution: Length of red-spotted beans. Serial numbers as in Fig. 4982. (Data from De Vries.)

The definition and formula indicate the process by which this quantity is found. Take the square of the deviation of each class, multiply it by its frequency, add the results, divide the sum by N, and extract the square root; all of which is performed easily by the aid of a table of logarithms. An example is given in the sixth column of the preceding table.

A third measure of variability, formerly much used, is the *probable deviation*. It might be called the median deviation, because the deviations that are greater and those that are less than it are equal in number. Galton (1889) has pointed out a method by which it may be obtained graphically from a polygon of distribution, as in Fig. 4983. Using the method employed in finding the median, find the values of the percentile grades at twenty-five and seventy-five per cent., and take half

their difference. This will be the probable deviation. It is found as easily and perhaps more exactly by multiplying the standard deviation by 0.6745. PE = 0.6745 σ.

The probable, or median deviation, corresponds to the so-called "probable error" of the mathematicians, and the standard deviations to the "error of mean squares." If we imagine a polygon of frequency to be a horizontal bar loaded with weights proportional to the ordinates and swinging about the mean, which will be the centre of gravity, then the standard deviation corresponds to what physicists call the "radius of gyration," or "swing radius."

It is found by the theory of probability that when $\sigma = 1$, AD = 0.7979, and PE = 0.6745. Thus we see that of the three measures of variability, the standard deviation is the largest. It has also the advantage of being the one most frequently used in mathematical investigations.

It has in common with the other two, however, the disadvantage of being expressed in units of measurement —inches, pounds, etc.; so we cannot compare, for instance, the variability of weight with that of stature while using this measure. A similar difficulty arises with organs of different size. In a thousand men from New York City, for example, we should find the standard deviation of their stature to be several inches, while that of the length of the nose would be only a fraction of an inch. But it would not be fair on that account to regard the noses as so much less variable than the statures.

So it has been proposed to use an abstract quantity called the *coefficient of variability*. This is obtained by dividing the standard deviation by the mean and multiplying by one hundred, as in the formula: $CV = 100 \frac{\sigma}{M}$.

In other words, it is the standard deviation expressed as a percentage of the mean. It is frequently useful as a means of comparing variabilities; but, unfortunately, it is not universally applicable, as it gives fallacious results when the data are in the form of ratios or in degrees of an angle, and probably in other cases.

Theoretical Curves.—Having obtained the mean and the standard deviation, we know the type and amount of variability of the material at hand. The plotted polygon of frequency gives a visual idea of the distribution of frequencies on either side of the mean, and with the aid of the median we are able to determine roughly whether the distribution is symmetrical or skew. Taking these results of observation as premises, the next step

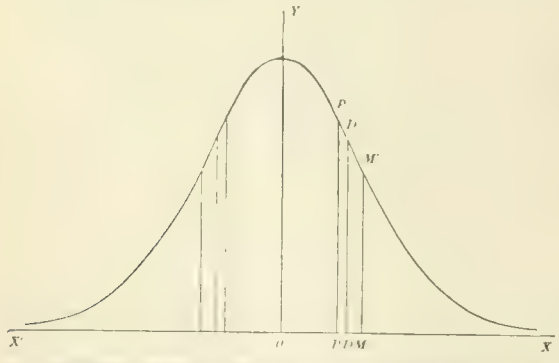

FIG. 4984.—The Normal Curve of Frequency. YO, ordinate of the mean; OP, "probable" deviation; OD, average deviation; OM, standard deviation. (From Bartlett.)

is to construct a theory as to the most probable distribution of the variations in the whole population, of which our material is a sample.

In a previous section, we have seen how close the variations in number of spots in throws of dice correspond to the theoretical probability as expressed by the formula $N(p+q)^n$ when this binomial is expanded, and comparison of the polygons (Figs. 4978, 4979, 4981, and 4982) seem to indicate that the same method is applicable with organic variations. It may be used with discrete variations where there are few classes; but in nature N,

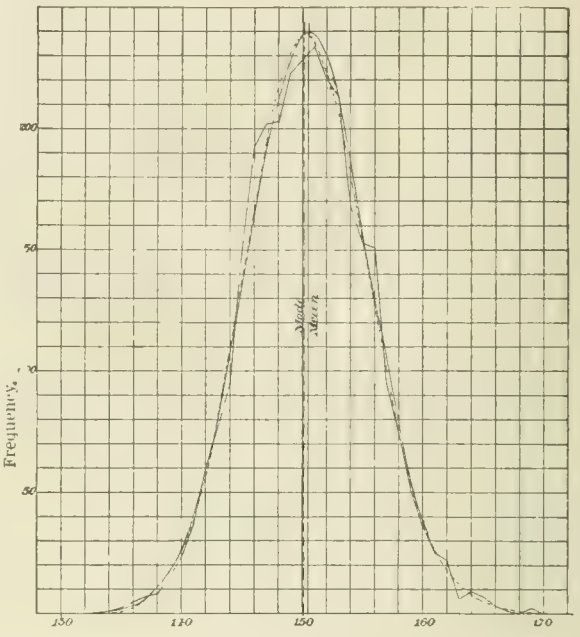

FIG. 4985.—Frequency of the Variations in Breadth of Head of 3,000 criminals. Irregular line, polygon of frequency. Normal curve —; skew curve of Type IV – – – –. (From Macdonell.)

p, q, and n are all unknown quantities, and with conjacent variations the division into classes is purely arbitrary. So it is better to employ a method that will give a continuous theoretical curve, such as would be obtained if, in the formula $(p+q)^n$, n were infinitely large.

Now it was shown long ago by Quetelet, Galton, and others that variations in human stature and in other characters follow closely the law expressed by the "normal curve of error" of the mathematicians, or what we should call the *normal curve of frequency* (although other curves more often fit the polygons of organic variation). This is a flowing curve (Fig. 4984), symmetrical about the mean, and theoretically without limit at the ends. The standard deviation marks the point of inflection on the sides. The formula for the curve is $y = y_0 \frac{1}{e^{x^2/2\sigma^2}}$, in which y is any ordinate, x is the corresponding abscissa, or deviation, measured from the ordinate of the mean, or "centroid verticle," y_0 is the height of this ordinate, σ is the standard deviation, and e is the basis of the Napierian system of logarithms, in which $e = 1 + \frac{1}{1} + \frac{1}{1\times 2} + \frac{1}{1\times 2\times 3} + \ldots$ etc. = 2.7182818. The meaning of the formula is, of course, that for any value of x the corresponding value of y will satisfy this equation.

If in our material we find the distribution of variations to be very nearly symmetrical, as in the beans, where the difference between mean and median is only 0.01 mm., we may assume that the normal curve will give the correct theoretical values, and may proceed at once to test this by fitting a normal curve to the observed polygon in the following manner: The mean (M) and the standard deviation (σ) have been found, and in doing this we have found also x_1, x_2, x_3, etc., which are the deviations from

the mean of classes 1, 2, 3, etc. Next find the height of the maximum ordinate. This operation is indicated by the formula $y_0 = \frac{N}{\sigma\sqrt{2\pi}}$, in which N = total number of observations and $\pi = 3.14159$. Now turning to Davenport (1899, p. 54) we find a table of the ordinates of the normal curve in which the "argument" is $\frac{x}{\sigma}$ and the corresponding tabular entry is $\frac{y}{y_0}$. So we must find $\frac{x}{\sigma}$, that is, divide the deviation of each class by the standard deviation. Then in the table find the tabular entry corresponding to each value of $\frac{x}{\sigma}$, interpolating, if necessary, and multiply the value thus found by y_0. The result will be the height of the ordinate of the theoretical curve upon the scale of frequency used in constructing the polygon. When these ordinates are plotted and their tops connected by a flowing curve, we have the theoretical curve (as in Fig. 4985), that is, a graphic representation of the distribution of the frequencies of the variations in nature, based upon the sample observed and the assumption that the variations follow the law of probability with $p = q$, and $n = \infty$.

This is the simplest of all the methods for fitting a theoretical curve to an observed polygon. It is especially applicable for discrete variations when the distribution of frequencies is symmetrical. It may be used also, but with less accuracy, for similar polygons of conjacent variations by taking the mid-value of each class as the position of its ordinate.

For greater accuracy with conjacent variation and in all cases of skew variation it is necessary to employ a more complicated procedure, the foundations of which have been laid by Pearson (1896, 1901, 1902). This is the *method of moments*. We return to the analogy between the polygon of frequency and a light rod loaded with balls suspended from it at regular intervals. The tendency of a ball to bend the rod will depend upon the weight of the ball and its distance from the point of support. The product of this distance multiplied by the weight is the *moment*, or first moment, of the ball about the point of support. The square of the distance multiplied by the weight gives the second moment, the cube, the third moment, and so on. Applying this principle to the polygon of frequency, we proceed at once to calculate the first, second, third, and fourth "rough moments" of the polygon as a whole about any convenient ordinate. From these rough moments it is easy to calculate the mean and the moments about the mean. These give us the standard deviation, and by their combination we are able to calculate the skewness and determine the general form of the curve. The actual calculation of the ordinates necessary to plot the curve is quite a different matter.

In practice it is best to use the serial numbers of the classes as their values, then taking the value of a class near the middle as V_m we find the deviations $-x_1$, $-x_2$, $-x_3$, and $+x_1$, $+x_2$, $+x_3$, etc. Then multiplying by their frequencies (z) and adding, being careful to regard the signs, we get a sum which divided by the total number of observations gives $\nu_1 = \frac{\Sigma(zx)}{N}$, which is the first rough moment of the curve about V_m with the frequencies of the classes grouped about their midordinates. In the same way we find the second, third, and fourth moments:

$$\nu_2 = \frac{\Sigma(zx^2)}{N}, \quad \nu_3 = \frac{\Sigma(zx^3)}{N}, \text{ and } \nu_4 = \frac{\Sigma(zx^4)}{N}.$$

Now in the theoretical curve the classes are not represented by rectangles but by trapezia, whose centres of gravity are not on the midordinates (Goodman, 1899, p. 60). This is allowed for and we find the corrected moments about V_m by use of the formulæ (Pearson, 1902*b*, pp. 287–289).

$$\mu_1 = \nu_1$$
$$\mu_2 = \nu_2 - \frac{h^2}{12}$$
$$\mu_3 = \nu_3 - \frac{h^2}{4}\nu_1$$
$$\mu_4 = \nu_4 - \frac{h^2}{2}\nu_2 + \frac{7}{240}h^4.$$

In these formulæ h is the distances apart of the ordinates and, if we use the serial numbers, $h = 1$.

Now we can find the mean from V_m by adding or subtracting μ'_1, after substituting the true values for those derived from the serial numbers, *i.e.*, $M = V_m - \mu'_1$.

Now the moments of the curve about M will be found as follows (*loc. cit.*, p. 283):

$$\mu_1 = 0$$
$$\mu_2 = \mu_2' - \mu_1'^2$$
$$\mu_3 = \mu_3' - 3\mu_1\mu_2' + 2\mu_1'^3$$
$$\mu_4 = \mu_4' - 4\mu_1\mu_3' + 6\mu_1'^2\mu_2' - 3\mu_1'^4.$$

The square root of the second moment is the standard deviation, $\sigma = \sqrt{\mu_2}$.

Now that we know the mean, or *centroid*, the standard deviation, or swing radius, and the moments of the curve about the centroid, we are prepared to determine the form of the curve.

If $\mu_3 = 0$ and $\mu_4 = 3\mu_2^2$, the curve is normal. If these equations are not true, the curve is skew and we may proceed to discover whether it will have a range limited at both ends, limited at one end only, or an unlimited range

TYPES OF FREQUENCY CURVES

Type.	Description.	Formula.	Criterion κ_1.	Criterion κ_2	References. Pearson.
Normal..	Symmetrical. Range unlimited. (Figs. 4984 and 4985.)	$y = y_0 \frac{1}{e^{\frac{x^2}{2\sigma^2}}}$	$\kappa_1 = 0$ $\beta_1 = 0, \beta_2 = 3$	$\kappa_2 = 0$	
I.....	Skew. Range limited both ends.	$y = y_0 \left(1 + \frac{x}{a_1}\right)^{m_1} \left(1 - \frac{x}{a_2}\right)^{m_2}$	$\kappa_1 < 0$ $\beta_1 > 0$	$\kappa_2 < 0$	'96, p. 367. '01 (b), p. 444.
II.....	Symmetrical. Range limited both ends.	$y = y_0 \left(1 - \frac{x^2}{a^2}\right)^m$	$\kappa_1 < 0$ $\beta_1 = 0, \beta_2$ not $= 3$	$\kappa_2 < 0$	'96, p. 372.
III.....	Skew. Range limited at one end. Transition form. (Fig. 4986.)	$y = y_0 \left(1 + \frac{x}{a}\right)^{\gamma a} e^{-\gamma x}$	$\kappa_1 = 0$ $\beta_1 > 0, \beta_2 > 3$	$\kappa_2 \propto$	'95, p. 373.
IV.....	Skew. Range unlimited. (Fig. 4985.)	$y = \frac{y_0}{\left(1 + \left(\frac{x}{a}\right)^2\right)^m} e^{-\nu \tan^{-1}\left(\frac{x}{a}\right)}$	$\kappa_1 > 0$ $\beta_1 > 0, \beta_2 > 3$	$\kappa_2 > 0$ & < 1	'96, p. 376.
V.....	Skew. Range limited at one end. Transition form.	$y = y_0 x^{-p} e^{-\gamma x}$	.....	$\kappa_2 = 1$	'01 (b), p. 446.
VI.....	Skew. Range limited at one end.	$y = y_0 \frac{(x-a)^{m_1}}{x^{m_2}}$	.....	$\kappa_2 > 1$ & < 2	'01 (b), p. 448.

by calculating the value of $2\mu_2(3\mu_2^2 - \mu_4) + 3\mu_3^2$. If this quantity is greater than zero the range is limited at both ends; if equal to zero, it is limited at one end only; and if less than zero, it is unlimited.

Pearson has distinguished seven types of curves of frequency, the descriptions and formulæ of which are given in the preceding table. In order to determine to which type our curve belongs we must find the values of the following quantities:

$$\beta_1 = \frac{\mu_3^2}{\mu_2^3}, \quad \beta_2 = \frac{\mu_4}{\mu_2^2}, \quad \kappa_1 = 2\beta_2 - 3\beta_1 - 6,$$

$$\text{and } \kappa_2 = \frac{\beta_1(\beta_2+3)^2}{4\kappa_1(4\beta_2 - 3\beta_1)}.$$

We may call κ_1 and κ_2 the first and second *criteria*. Looking up these values in the table we find there the formula for the curve, from which the ordinates may be calculated. The second criterion serves to differentiate all of the curves except the normal and Type II., in both of which $\kappa_2 = 0$, but Type II. differs from the normal in that β_2 is not equal to 3. The ordinates of the normal curve may be calculated by the aid of the improved tables given by Sheppard (1903), but for the other curves there are no such tables. It would unduly expand this article if we should attempt to explain fully the formulæ for Types I. to VI. and give directions for calculating the values of y, and must, therefore, refer the reader for further details to Pearson's original articles (1896, 1901, and 1902). It should be noted, however, that our curve may be regarded as normal, even if it does not quite satisfy the conditions given in the table. According to Dunker (1899, p. 134), if the product of κ_1 multiplied by by μ_2^3 is within the limits of ± 1, and the value of $\frac{3\beta_2 - 2\beta_1 + (+\frac{1}{10})}{\beta_1}$ is between 0.8 and 1.25, unity being the value with a strictly normal curve, we may still regard our curve as of the normal type.

Skewness is measured by the deviation (d) of the mean from the mode expressed in terms of the standard deviation. Thus $\text{Sk} = \frac{d}{\sigma}$. When the value of the mean is greater than the mode, the skewness is said to be positive; when less, negative. The skewness is calculated by a different formula for each type of curve. But it is not difficult to estimate it by the rule given previously for estimating the mode, if we know the mean, median, and standard deviation.

In fact, there is considerable doubt as to how far mathematical analysis of the statistics of variation can be carried with profit. The types of curves grade into one another in such a way that it may happen that in some cases either one of two or more curves will fit the polygon equally well for practical purposes. Thus Miss Hefferan (1900) found a case in which dropping out one extreme individual in a series of four hundred changed the curve from Type IV. to Type I., and the two curves when plotted are practically identical. Pearson (1901, p. 453) gives a case in which two curves of Types V. and VI. plotted from the same data are so close as to be hardly distinguishable to the eye.

Correlation of Variations.—So far we have dealt with variations of single characters only. But every organism possesses many characters and organs, and these are related in many ways, both as to structure and function. Now there may or may not be some definite relation on the average between the variations of any given pair of associated characters.

In the language of Galton (1889): "Two variable organs are said to be correlated when the variation of the one is accompanied on the average by more or less variation of the other, and in the same direction." This is *positive correlation*. When the variation of the second organ is in the opposite direction from that of the first, we have *negative correlation*. Many correlations are matters of every-day observation. Thus the right leg is generally of very nearly the same length as the left leg. There is a similar but less close correlation between the lengths of arms and legs, a man with light hair usually has blue eyes, and so on.

We may find correlations also between similar characters in associated individuals, as fathers and sons (see *Heredity*), or husbands and wives; also between characters of organisms and factors in their environment or their previous treatment or condition, as between color of plumage and latitude of habitat, susceptibility to disease and age, immunity against smallpox and vaccination.

Such correlations are clearly of great theoretical importance for the study of evolution and heredity, and they have very practical bearings upon medical and social questions.

Therefore it is important that we should have some means of expressing the amount of correlation in quantitative terms. This means has been furnished by Galton (1889) who showed how to find the *coefficient of correlation*, or what is often called Galton's function.

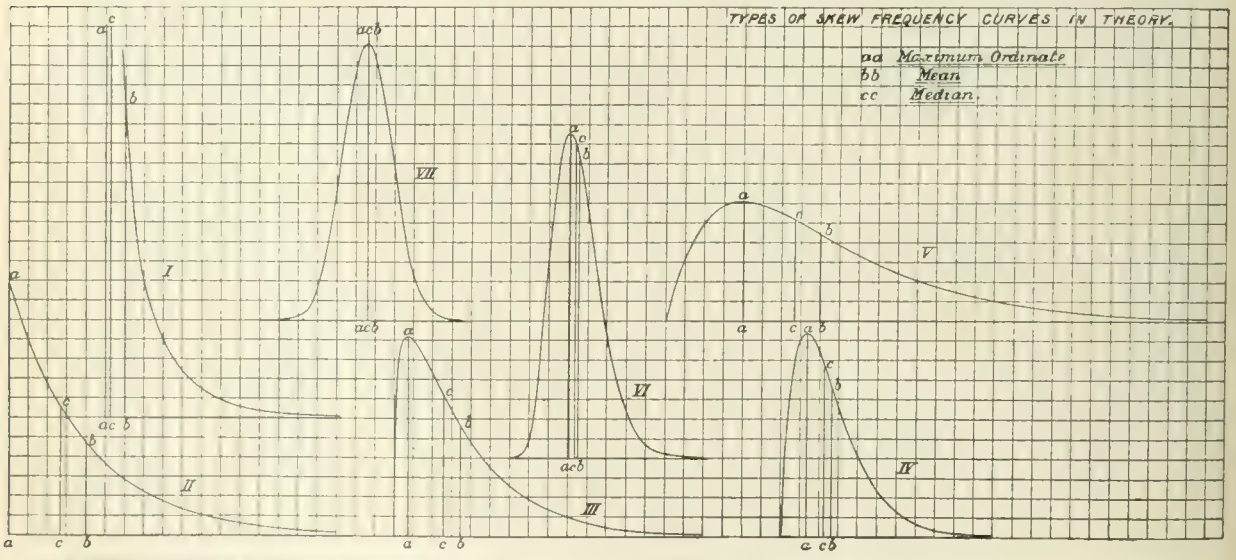

FIG. 4986.—The Various Sub-Types of Transitional Skew Frequency Curve of Type III. *aa*, Maximum ordinate; *bb*, ordinate of the mean; *cc*, ordinate of the median. (From Pearson.)

Suppose we have measurements of the length and breadth of the heads of one thousand men. The data may be arranged in a *correlation table*, like the one given below. This is constructed in the following manner: At the top is a horizontal scale of length, and we will call this the selected character, or "subject." Likewise at the left is a vertical scale of breadth, which is the associated character, or "relative." The entries in the body of the table are the frequencies of individuals in which this pair of characters have the values given in the corresponding positions in the horizontal and vertical scales, respectively. For example, there were 21 men whose head length was 7.1 inches. Of these 1 had a width of 5.7 inches, 4 were 5.8, 4 were 5.9, 6 were 6 inches broad, and so on. The columns and rows of frequencies are added up at the bottom and at the right. Each column forms an *array*, which shows the variations of breadth associated with the value of the length given at the head of the column. In the same way breadth may be taken as the subject, and then the rows of frequencies are the arrays, giving the variations of the associated length.

Correlation Table. Head Length on Head Breadth. 1,000 Cambridge Men. (From Macdonell.)

Head Breadth (Inches).	Head Length in Inches																		Totals.
	6.8	6.9	7	7.1	7.2	7.3	7.4	7.5	7.6	7.7	7.8	7.9	8	8.1	8.2	8.3	8.4	8.5	8.6	
5.5	..	.	.	.	1	.	2	.	.	.	.	.	.	.	.	.	.	.	.	3
5.6	..	.	.	.	2	3	1	4	2	.	.	.	.	.	.	.	..	..	..	12
5.7	1	1	.	1	2	6	5	7	5	8	3	4	.	.	.	.	..	.	.	43
5.8	..	..	2	4	6	7	15	12	12	11	7	3	1	.	.	.	..	..	.	80
5.9	..	.	1	4	6	16	16	24	20	28	7	5	4	.	.	.	..	..	.	131
6.0	..	1	.	6	14	12	24	40	45	40	23	9	13	4	.	.	..	..	..	236
6.1	..	..	1	3	4	6	11	27	42	40	32	15	10	2	2	.	..	..		185
6.2	..	.	1	2	6	3	14	18	22	25	13	14	17	2	4	1	..	..	..	142
6.3	..	..	1	..	1	4	9	8	16	15	15	16	6	1	..	..	..	..	1	99
6.4	..	.	..	..	1	..	2	4	6	6	3	4	7	2	1	1	..	..	.	37
6.5	.	.	.	.	.	1	1	.	3	3	.	2	3	1	1	.	..	..	.	15
6.6	..	.	.	1	.	.	.	1	2	3	.	1	.	2	1	1	..	.	.	12
6.7	..	.	..	.	.	.	.	.	.	1	.	.	.	2	.	..	..	..		3
6.8	..	.	.	.	.	.	.	.	.	.	.	2	.	.	.	.	.	.	.	2
Totals.	1	2	6	21	43	58	100	145	175	180	98	75	61	22	9	3	..	..	1	1,000

The means and standard deviations of the subject and relative may be calculated from the total frequencies given at the bottom and right side of the table, respectively, by the methods previously described. In the same way the mean may be determined for each array. Now transferring our horizontal and vertical scales to plotting paper, the positions of the means of the arrays may be plotted as in Fig. 4987, which is made from a correlation table of head breadth and stature in three thousand criminals. In this diagram the position of the mean of an array, is indicated by a small circle, and the

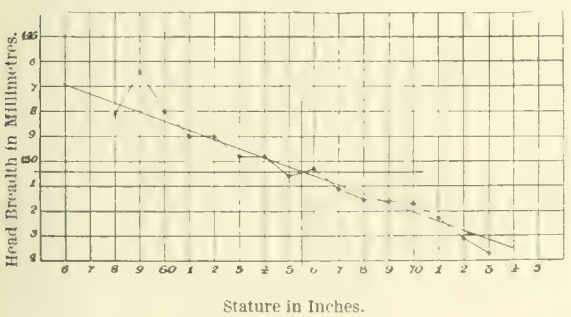

Fig. 4987. Diagram of Correlation Table. Stature, subject; head breadth, relative. Three thousand criminals, mean height = 65.5 inches, mean head breadth = 150.4 mm. Coefficient of regression = 0.3612. (From Macdonell.)

circles are connected by a zigzag line. The position of the mean of all the statures is represented by a vertical line drawn through the middle of the diagram: call this the axis of x; and the position of the mean of all the head breadths is similarly represented by the intersecting horizontal line, the axis of y. Now the horizontal distance of a circle from the axis of x will give the deviation (x) of the selected character, and the vertical distance of the same circle from the axis of y will give the mean deviation (y) of the associated array from the mean of all the arrays. Now if x and y are expressed in equivalent units, the ratio $\frac{y}{x}$ will give a measure of the correlation of the two characters in this particular array. If the ratio $\frac{y}{x}$ were the same in all the arrays, the zigzag line in Fig. 4987 would become a straight line. As it is, we see that it has a general trend which is represented by a straight line that may be drawn so that the sum of the distances of the small circles from it shall be as small as possible. This line will meet the axes of x and y at their point of intersection. Now the slope of this line may be measured in the same way that the grade of a railway track is measured, by the rise or fall in a certain unit of horizontal distance, as ten feet in a mile, or in our case by the height y_a of any point a at the distance x_a from m_1 (Fig. 4988). The slope of the line may be

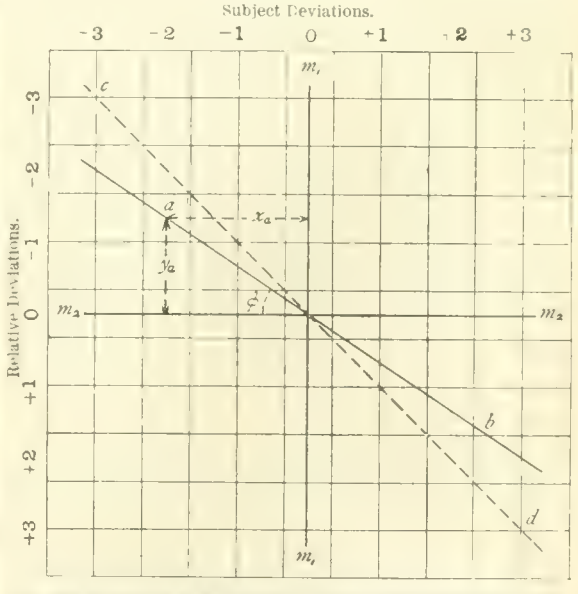

Fig. 4988. Diagram of a Correlation Table with Deviations Plotted in Terms of Standard Deviation. m_1, Position of mean of subject; m_2, mean of relative; $a\ b$, regression line.

measured also by the angle ϕ which it makes with the line m_2, and the ratio $\frac{y_a}{x_a}$ is what mathematicians call the tangent of that angle, $\frac{y_a}{x_a} = \tan \varphi$. It may be shown by the principle of least squares that, taking all the observations into consideration, the most probable value of tan ϕ will be $\tan \varphi = \frac{\Sigma (x\ y\ z)}{\Sigma (x^2 z)}$, where x and y are the deviations of each pair of observations from the means of the subject and relative, respectively, z is the number of pairs, or frequency of each class in the arrays, and Σ is the sign for summation. But in a diagram like Fig. 4987 the ratio $\frac{\Sigma (x\ y\ z)}{\Sigma (x^2 z)}$ will not give a constant measure of the correlation between the two characters, because, in the first place, x is expressed in inches while y is in millimetres. If we changed these units, we would change the ratio. Moreover, stature and head breadth have different standard deviations, so that the diagram is longer in one direction than in the other, and the slope of the diagonal would differ according as to whether head breadth or height were taken as the subject.

Galton overcame this difficulty by expressing all the deviations of each character in terms of its probable deviation. Then his correlation table took the form represented in Fig. 4988, when $\frac{y_a}{x_a}$ gives the coefficient of correlation no matter which character is taken as subject. If there is perfect correlation the line *ab* will coincide with *cd* and $\frac{y_a}{x_a} = 1$. But if there is no correlation *ab* coincides with m_2 and $\frac{y_a}{x_a} = 0$. So the coefficient of correlation is a fraction which may have any value between 0 and 1, in Fig. 4988 its value is $\frac{2}{3}$, and, if A be the selected character and B the relative, then this coefficient expresses the probable proportion of the mean deviation of B to the corresponding selected deviation of A. In general the deviations of B will be found to be less than the corresponding deviations of A. Galton first noticed this phenomenon in his early studies of heredity and he called it *regression*.

But regression is not peculiar to heredity. It is found in all statistics concerned with two associated variable quantities which are not perfectly correlated. What we mean by regression, then, is "that in associated or correlated pairs, if we select one member with a given value for its character, the second has on the average a less value, regressing somewhat to the mean of the general population" (Pearson, 1900, p. 394). Regression is thus the reverse of correlation.

In a diagram like Fig. 4987, in which the positions of the means of the arrays are plotted in the units of actual measurement, the zigzag line drawn through the means is called the *polygon of regression*, and the straight line that best fits this polygon is called the *line of regression*. For want of a better name, the slope of the line of regression has been called the *coefficient of regression*, although it does not measure regression directly, but inversely. It is a peculiarly unfortunate choice of name, because it has led to much confusion and misunderstanding through the natural tendency of recent writers to speak of it simply as "the regression."

We have seen that the slope of the regression line is given by the ratio $\frac{\Sigma (x\ y\ z)}{\Sigma (x^2 z)}$. But $\Sigma (x^2 z) = N\sigma_1{}^2$ and we may make $\Sigma(xyz) = Nr\sigma_1\sigma_2$, where N is the total number of pairs, σ_1 the standard deviation of the subject, σ_2 the standard deviation of the relative and r is an unknown quantity. Then $\frac{\Sigma (x\ y\ z)}{\Sigma (x^2 z)} = \frac{Nr\sigma_1\sigma_2}{N\sigma_1{}^2} = r\frac{\sigma_2}{\sigma_1}$. Thus the formula for the *coefficient of regression* becomes $r\frac{\sigma_2}{\sigma_1}$, and then it may be shown that $r =$ the *coefficient of correlation*. They both measure the same phenomenon. The former gives the probable ratio of the deviations as they are actually observed. The latter gives a corrected value of this quantity after due allowance has been made for differences in units of measurement and in standard deviation. In cases in which $\sigma_1 = \sigma_2$, then $\tan \phi = r\frac{\sigma_2}{\sigma_1} = r$.

There is one more property of the correlation surface, as it is called, that should be noted. If x and y are plotted in terms of σ_1 and σ_2, as in Fig. 4988, and the distribution of frequencies is normal, then when $r = 0$, a series of contour lines drawn through the classes of equal frequency will be perfect circles. When the regression line, *ab*, moves from m_2 toward *cd*, the contour lines become ellipses with *cd* as their major axis. As *ab* approaches *cd* the ellipses become more and more narrow until when *ab* coincides with *cd*, that is, with perfect correlation, the frequency of each array would be concentrated along the line *cd*. Now the range of each array is measured by its standard deviation, which with perfectly normal distribution would be given by the formula $\sigma_3 = \sigma\sqrt{1 - r^2}$. It is evident that as r approaches the value of 1, $1 - r^2$ will become smaller and smaller until finally $\sigma_3 = 0$, that is, until the distribution of frequencies of the arrays is concentrated along the major axis of the ellipses. This shows that the accuracy with which one can use the value of a character to predict the value of its associated character will depend to a great extent upon the amount of correlation existing between them.

There are two methods at present in use for calculating the coefficient of correlation. The first method depends on the formula $r = \frac{\Sigma (x\ y\ z)}{N\sigma_1\ \sigma_2}$, which has been shown by Pearson to give the best value for r. The formula indicates the method of procedure, which is simple but laborious. Having constructed a correlation table and found the means and standard deviations of subject and relative, the deviations x and y for each array class are found, and then multiplied together and by the frequency of the class. All these products are added and the sum is divided by the product of the whole number of pairs multiplied by the standard deviations of subject and relative. The result is the coefficient of correlation.

Dunker (1899, p. 154) has devised a modification of this method, which is intended to lessen the labor, and is fully described by Davenport (1899, p. 33).

The second method is more complex in theory, but is shorter in practice. Theoretically it is not so good as the first, but it has the advantage of saving a great deal of time and labor, and it is the only method that can be used with characters that are not quantitatively measurable. It was for this purpose that the method was invented by Pearson (1901). Macdonell (1902) has made a careful comparison of the two methods, and concludes that the new method gives a value of r with an accuracy fairly comparable to that obtained from an ordinary frequency table containing about one-third the number of frequencies. The results obtained in three cases by the two methods are compared in the following table:

Comparison of the Two Methods.

	Coefficient of Correlation.	
	First method.	Second method.
Head length and head breadth	.4016 ± .0103	.3977 ± .0176
Head breadth and stature	.1831 ± .0119	.1811 ± .0210
Left middle finger and stature	.6608 ± .0069	.6633 ± .0142

The theory of this second method is explained in untechnical language by Pearson in the "Grammar of Science" (1900, pp. 432–436). We will proceed at once with a description of the manner in which the theory is applied in the calculation of r.

The material is arranged in a fourfold correlation table like the following:

CORRELATION OF STATURE AND BREADTH OF HEAD. 3,000 CRIMINALS. (Macdonell.)

Head breadth (centimetres).	Stature in Feet and Inches.		Totals.
	5′ 4$\frac{9}{16}$″ and under.	Over 5′ 4$\frac{9}{16}$″.	
14.8 and under	455	622	1,077
Over 14.8	599	1,324	1,923
Totals	1,054	1,946	3,000

CORRELATION OF PREVIOUS TREATMENT AND RESULT OF SMALLPOX. HOMERTON AND FULHAM HOSPITALS (DOUBTFUL CASES EXCLUDED). (Macdonell.)

	Recoveries.	Deaths.	Totals.
Vaccinated	8,207	692	8,899
Unvaccinated	1,424	1,103	2,527
Totals	9,631	1,795	11,426

Let the correlation table be represented by the following diagrams:

TABLE OF FREQUENCIES.

a	b	$a+b$
c	d	$c+d$
$a+c$	$b+d$	N

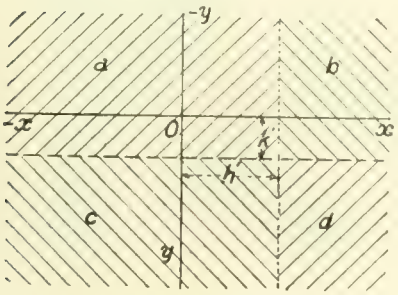

FIG. 4989.—Diagram Showing the Theoretical Relation of the Table of Frequencies to a Normal Correlation Surface. The shaded rectangles a, b, c, d represent the divisions of the table of frequencies, h' and k' the deviations of the lines of division from the means of subject and relative represented by the axes of y and x. (From Pearson.)

Calculate the values of a_1 and a_2 by the formulæ

$$a_1 = \frac{(a+c)-(b+d)}{N}.$$

$$a_2 = \frac{(a+b)-(c+d)}{N}.$$

Now we need a table of the "probability integral," which gives the "sums from the beginning" of the normal curve of frequency. In "Biometrika," vol. ii., pp. 182–190, is a series of tables of this kind prepared especially for our purpose. Turning to Tables III. and IV., pp. 189–190, we find in the a column our value of a_1 and in the x column read off the corresponding tabular entry, interpolating if necessary, and the value thus obtained is called h. Continuing to the z column we find the tabular entry and call that H. In the same way for a_2 we find the corresponding entries under x and z and call them k and K.

Then find ε by the formula $\varepsilon = \frac{ad-bc}{N \cdot H K}$, and r, the coefficient of correlation, may be found from the equation,

$$r = \varepsilon + \frac{\varepsilon^2}{2} hk + \frac{\varepsilon^3}{6}(h^2-1)(k^2-1) + \frac{\varepsilon^4}{24} h(h^2-3)k(k^2-3) + \ldots \text{etc.}$$

(Pearson, 1901*a*, p. 6).

Or, if we wish to be a little more exact, we may find r by the following equations:

$$r = \theta + \tfrac{1}{2} hk\theta^2 - (h^2+k^2-hk)\frac{\theta^3}{6} + hk\left(h^2k^2 - 3(h^2+k^2) - 5\right)\frac{\theta^4}{24} + \text{etc.}$$

$r = \sin\theta$ (Fig. 4990). (Pearson, *loc. cit.*, p. 8.)

The equations for finding r and θ may be solved by Newton's method of approximation, or better by Horner's method (see Wells, "College Algebra," p. 520); or Burnside and Panton, 1892, p. 212). In the second equation the value of the angle θ is given in radians, ratio of arc to radius. As $\frac{1}{2}\pi = 90°$, the value of θ in seconds is given by the equation $A = 206{,}265\ \theta$ (De Morgan, 1902, p. 276). Reducing A to degrees, minutes, and seconds, $r = \sin\theta$ is found easily in any table of natural sines (*e.g.*, Jones, "Logarithmic Tables," pp. 60 *et seq.*). A still easier method of finding r from θ is to take a table like Jones's Table II. (*loc. cit.*, pp. 15–19) where the angles are given both in degrees and in radians, and $\log r = \log \sin\theta$ can be read off directly, and r, found from a table of logarithms.

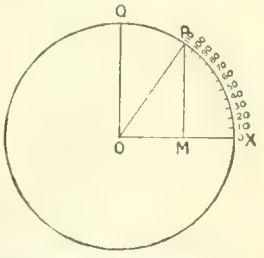

FIG. 4990. Illustrating the Meaning of $r = \sin\theta$. If the angle $POX = \theta$ is measured by the arc PX, then $r = \sin\theta = PM$, OP being taken as unity. (From Pearson.)

Pearson has given (1902 *b*, pp. 13–14) a graphical method for fitting a straight line to a set of observations that seems applicable in the plotting of regression lines and the calculation of coefficients of correlation. But it is doubtful if this method would have any advantage over the one just described.

It will be interesting to note at this point some of the results that have been obtained by the study of correlation. The following coefficients of correlation were obtained by Macdonell from three thousand criminals:

CORRELATIONS	COEFFICIENT.
Stature and head length	0.33993
Stature and head breadth	.18308
Stature and face breadth	.34527
Stature and finger	.66084
Stature and cubit	.79986
Stature and foot	.77636

From the results of which these form a part he has arrived at important conclusions concerning the identification of criminals.

Some correlations of especial interest to physicians are:

DIPHTHERIA. Pearson (1901)—Correlation of antitoxin treatment and recovery ..... $r = 0.2451 \pm 0.0205$

SMALLPOX, Macdonell (1902)—Effectiveness of vaccination and strength to resist the disease.

For six towns	$r = 0.6561 \pm 0.0092$	
For Sheffield	.7694 ± .0124	Doubtful cases included in the vaccinated.
For Leicester	.6112 ± .0728	
For Gloucester	.5897 ± .0198	
For Homerton and Fulham	.5760 ± .0089	
For Homerton and Fulham	.6615 ± .0083	Doubtful cases excluded.
For Glasgow	.7783 ± .0365	
For London, 1901	.5779 ± .0311	
For London, 1892-93	.5954 ± .0272	

Precision of the Constants.—The constants of our curves of variation and correlation—mean, median, standard deviation, coefficient of correlation, and the like—are

the predictions made from observations as to the probable condition of the given character in the whole population. Our data are like the balls drawn from the urn which we cannot see into nor upset. We can only guess at what is in the urn by what has been drawn out of it. We have seen that the probability of our guess being right depends upon the number of observations. This is expressed by the, so-called, probable errors of the constants, which, preceded by the ± sign, are written after the constants, as in the examples given in previous sections. We will now give the formulæ for calculating the probable errors (P.E.) of some of the most important constants. When distribution is normal:

$$\text{P. E. of mean} = .6745\frac{\sigma}{\sqrt{N}}.$$

$$\text{P. E. of median} \quad .8454\frac{\sigma}{\sqrt{N}}$$

$$\text{P. E. of } \sigma \quad .6745\frac{\sigma}{\sqrt{2N}}.$$

$$\text{When } r = \frac{\Sigma(xyz)}{N\sigma_1\sigma_2}. \qquad \text{P. E. of } r = .6745\frac{1-r^2}{\sqrt{N}}.$$

When r is calculated by the second method, its P. E. has a very complex formula (Pearson, 1901, p. 14). But, according to Macdonell, it will be about the same as if r were calculated by the first method with one-third the number of pairs. Yule gives a table (1897, p. 854) of the P.E. of r by the first method for various values of N.

Biologists are indebted to Elderton for a useful table ("Biometrika," vol. i., part ii.), by which it is possible to determine whether the differences between a polygon of frequency and the corresponding theoretical curve are greater or less than the probability of random sampling should lead one to expect. If they are not greater, the curve chosen may be regarded as a satisfactory representation of the relative frequencies of the variations in nature.

We will now bring to a close this description of the methods employed in statistical biology, which we believe to be the first one that is both fairly complete and in a language that can be understood by the ordinary American biologist or physician; and we venture to express the hope that it may lead to a wider investigation in the fields that these new methods make available for study. *Robert Payne Bigelow.*

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VARICELLA. See *Chickenpox.*

VARICOCELE. See *Sexual Organs, Male, Diseases of.*

VARICOSE VEINS.—Etiology.—Dilated and tortuous veins are spoken of as varices, or varicose veins. This abnormal condition is dependent in some way upon an interference with the flow of blood in the veins. Thus gravity plays its part, since the trouble is most common in the veins of the legs, and since it is more often seen in tall people than in short ones. Age and disease of the heart, producing imperfect valvular action, are also potent factors. As instances of local venous obstruction may be mentioned abdominal tumors, pregnancy, and the wearing of constricting clothing, such as circular garters. The left spermatic vein empties into the left renal vein at a right angle, being crossed by the sigmoid flexure. The pressure exerted upon it by an accumulation of fæces is thought to be one reason why varicocele is common on the left side.

However, the reasons just stated are not of themselves sufficient to explain the occurrence of varicose veins. Thus the veins begin to dilate in the early months of pregnancy before the uterus is sufficiently enlarged to exert any pressure upon the iliac veins, while varicose veins are wanting in many patients with large abdominal tumors. Nor is the change due to the atrophy of old age, as it is usually noticed before the fortieth year, and in a great many instances before the twenty-fifth year. It is equally difficult to explain why the veins of one leg should be much dilated and tortuous, while those of the other are scarcely affected; or why in certain persons the large veins are chiefly affected, and in others the smaller radicles in the skin. As muscular contraction and muscular relaxation constitute the chief aids to venous flow, it is not surprising that persons who are obliged to stand for hours at a time (washerwomen, car motormen, etc.) suffer more from this trouble than those who are constantly changing their position.

Fig. 4991.—Varicose Veins of the Lower Limbs and Genital Organs in the Case of a Woman soon to be Delivered of her Tenth Child. (Duplay et Reclus: "Traité de Chirurgie.")

While any of the veins of the lower extremity may be affected, the trouble is most often found in some of the radicles of the internal saphenous vein. The tortuous and dilated vessels are easily recognized on inspection, and if they lie near the surface their bluish color is visible through the skin. If they are not or have not been inflamed, they collapse under moderate pressure and disappear almost entirely when the foot is elevated. In some places their channels through the skin feel like a break in its continuity; while here and there they lie so near the surface that they seem to be covered with little more than epithelium. The deep veins of the leg may be affected as well as the superficial ones. If the dilatation goes on to a still greater degree a distinct thin-walled sac filled with fluid blood is formed. Such a large varix is shown in Fig. 4992.

As a result of the dilatation many of the valves become insufficient. This can be tested in the following manner: After the veins of the lower extremities have been emptied by elevation of the foot and stroking of the limb toward the body, the thumb is placed upon the main saphenous trunk and the patient is directed to stand. The varicose veins will fill slowly and only to a moderate degree. The moment the thumb is removed the column of venous blood falling into them from above instantly distends them to their fullest capacity if the valves are incompetent. Such are the conditions of simple varicosity. Sooner or later one or more complications are likely to arise, such as thrombosis, rupture, periphlebitis, œdema, eczema, and ulcer.

Complications.—Thrombosis may occur in dilated veins of the leg exactly as it may occur in the dilated vein of an external hemorrhoid. It is accompanied by a good deal of pain and tenderness, by slight redness and by œdema plainly limited to the immediate vicinity of the vein involved. Thus if a not very tortuous vein be affected for a distance of five or six inches its course can be accurately mapped out as an indurated strip about three-fourths of an inch wide. If the vein is tortuous, the indurated area will have an irregular outline.

The nutrition of the parts drained by varicose veins is often seriously affected, so that a wound may become infected. The result may be erysipelas, cellulitis, abscess, or suppurative thrombophlebitis, although the last-mentioned condition is by no means common.

When the vein lies near the surface it is easily ruptured by a blow from a sharp object, and as there is little elastic tissue about the opening, the hemorrhage is profuse and may be serious if it is not stopped by pressure or ligation.

A fourth complication, more often seen in older individuals, is an extensive œdema. At first this is of the usual type, revealing itself by pitting on pressure; but after it has existed for many months the production of fibrous tissue may be sufficient to prevent much indentation on pressure. This condition may be due to other causes than varicosity of the veins, and it greatly interferes with the nutrition of the parts, and especially with the repair of a chronic ulcer, whether varicose or not.

Eczema is another complication due to an imperfect nutrition which is apt to lead to ulcers starting in the small scratches made by the patient in the vain attempt to relieve himself from the intolerable itching.

Not every ulcer occurring in a patient whose veins are varicose is to be attributed to such varicosity. A long-standing ulcer of the leg of a non-malignant, non-syphilitic, non-tuberculous character is better spoken of as a chronic ulcer. It may be the direct or indirect result of varicose veins, but it may also be due to traumatism or eczema, or œdema, or anæmia. It is misleading to call all such ulcers varicose ulcers. They are all due to poor local nutrition, of which varicosity of the veins is simply one cause.

When varicose veins have existed for a considerable time there will often be noted a brown pigmentation of the skin, occurring more or less in patches, and due either to small subcutaneous ruptures of the venous radicles or to transudation of red blood cells through the dilated venous walls. In either case the blood pigment becomes permanently fixed in the fibrous tissue of the skin, giving it a characteristic yellow-brown color.

Symptoms.—Varicose veins often give rise to no symptoms whatever. Such is apt to be the case in young and

Fig. 4992.—Varicose Veins of Both Legs with a Large Varicose Vein below the Left Knee and a Varicose Ulcer just above the Right Ankle. (Von Bruns.)

healthy persons, and also when the veins are dilated throughout a small area—for example, over one-half of the vulva, or around the saphenous opening.

The symptoms in uncomplicated cases are: A sense of weight and more or less dull aching relieved by elevation of the affected extremity.

The symptoms of thrombosis are: Marked tenderness on pressure, acute local pain, which is considerably but not wholly relieved by a recumbent position, and a rise of temperature of one, two, or three degrees.

The symptoms of the inflammatory complications mentioned above are such as accompany these processes wherever they occur in the body.

The Diagnosis of varicose veins and of the different complications above enumerated is easy for any one who is able to recognize the different forms of inflammation and ulceration. The inflamed strip of a varicose vein is broader than that of infection in a lymph vessel, and the overlying skin is not so red. A sharply localized varix can hardly be mistaken for any sort of a cystic growth, as it is collapsible on pressure, refills slowly, and has less tension than most cysts. It does not pulsate like an aneurism.

Treatment.—Palliative treatment of uncomplicated varicose veins consists in attention to the general health; in the avoidance of such occupations and such clothing as tend to interfere with the venous flow; in the elevation of the feet as much as possible when the patient is sitting down, and in the wearing, during the daytime, of an elastic bandage or stocking extending from the toes to the knee. Even though the varicose veins extend well into the thigh, firm compression of the leg will usually relieve the symptoms, and it is difficult to apply a stocking or bandage with comfort above the knee-joint.

A woven elastic, cotton or silk-web stocking costs from $2.50 to $8. Its advantages are the ease with which it may be applied and the firm pressure which it exerts when new. A thin white lisle thread stocking should be

worn next the skin to protect the elastic stocking from perspiration. With the best of care an elastic stocking loses its tone in a few months, so that the expense is no inconsiderable item to a poor person. Various kinds of elastic bandages have been devised, such as pure rubber, rubber webbing, cloth webbing, stockinette, etc., but nothing is more satisfactory than pure coarse white flannel cut on the bias in strips about three inches wide, a sufficient number of which are sewed together to make a bandage six or eight yards long. Such bandages can be washed and ironed as often as they become soiled, and they will last a long time. They should be applied before the patient gets up in the morning. In the beginning this is a considerable trouble, as it is by no means easy to bandage one's own leg. But most patients soon learn to apply them in five or ten minutes, and many put them on as neatly as a professional could hope to do. No one who has once become accustomed to apply such bandages would willingly exchange them for an elastic stocking, since he can always regulate the pressure according to his own comfort, aside from the fact that they are cleaner and cheaper.

The radical treatment of varicose veins may be (1) their multiple ligation, either subcutaneously or through short incisions, (2) the excision of portions or of the whole of the dilated veins, or (3) the double ligation of the saphenous vein at its entrance into the femoral. The injection of substances to produce clots in the veins is no longer in vogue.

The subcutaneous ligation of the vein consists in the passage of a needle threaded with catgut first beneath the vein and then between the vein and the skin (Fig. 4993).

The ligation of the main trunk of a saphenous vein was recommended by Trendelenburg in an article published in 1891. The good results then reported and those which have since been obtained by others, have given this operation a considerable renown. It is worth remembering, however, that a thrombus may form in the proximal portion of the vein and that it may reach up into the femoral and cause embolism. For this reason a patient ought to remain in bed for at least ten days after the operation. The vein can be exposed under the influence of cocaine at its termination in the femoral vein, or, in case its higher branches are not varicose, it may be exposed just below the centre of the thigh. It should be ligated in two places and divided between the ligatures.

The excision of a considerable length of a varicose vein is an operation which usually requires some little time

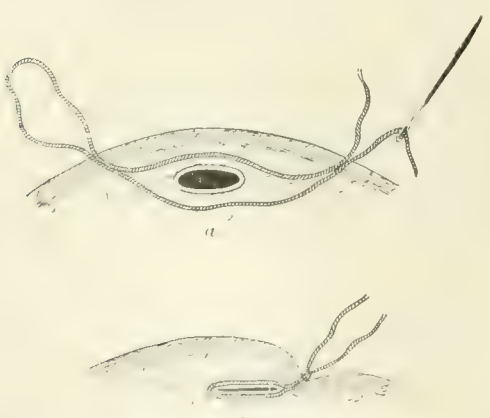

FIG. 4993. Subcutaneous Ligation of a Vein (Trendelenburg's Method). *a*, Shows how the ligature is to be applied; *b*, shows the condition of the parts after the ligature has been drawn taut and tied.

and which can best be performed under a general anæsthetic. The limb should be allowed to hang over the edge of the operating table for a minute or two for the purpose of distending the veins, and then a constricting band or rubber tube is placed around the thigh, not tight enough, however, to obstruct the arterial flow. The dissection of the veins should be made from above downward, since in this manner they will remain full of blood and will thus be easily found. As long as the vein is not cut into it is clearly visible and the dissection is easily performed; but often, in spite of his resolve not to do so, the operator will cut a hidden branch which extends from the superficial vein to some deeper one, and the wound will then become filled with a flow of blood which is sometimes stopped with difficulty. When the tissues are once stained with blood the veins are less easily recognized. When the affected veins have been removed the wounds in the skin are sutured, and if they heal primarily the patient should be able to go about in ten days or two weeks. The ultimate recovery is not hastened by getting the patient out of bed before there is firm union of the skin.

These operations are of service not only in relieving the patient of his troublesome varicose veins, but in tending to cure such complications as eczema and ulcer.

Excision may also be applied to a thrombosed vein. The time of recovery will not be much greater than that required for excision of an uncomplicated varicose vein, while the non-operative method of treatment of thrombosis often requires four or five weeks for effecting a cure. The risk is said to be no greater than that following excision of simple varicose veins.

The non-operative treatment of a thrombosed varicose vein consists in rest in bed and the application of moist wet dressings or an ice-bag to relieve the pain. In from two to four weeks the acute symptoms will have subsided, and the patient may again go about. It is better to apply, for a time at least, a firm bandage from the toes upward, so as to relieve the veins from the strain of a column of blood to which they have grown unaccustomed during the rest in bed. An annoying feature of thrombosis is its tendency to spread in spite of treatment. An extension upward along the vein may occur at any time, and the course of the trouble in the new situation will be exactly like that of the original thrombosis. Excision has been lately advised as a method of curing thrombosed veins, as stated above.

In regard to complications which may occur in connection with varicose veins, see articles on *Blood-Vessels, Pathological Anatomy of, Erysipelas, Phlegmon,* and *Ulcer and Ulceration.* *Edward Milton Foote.*

VARIX. See *Veins, Diseases of.*

VAS DEFERENS. See *Genital Organs, Male.*

VASO-MOTOR NERVES. See *Circulation of the Blood.*

VEINS, ANOMALIES OF.—The anomalies of veins, though of great morphological interest, are, with a few exceptions, of no great surgical importance. The most important variations of the venous system are found in the great veins entering the heart, and in their large tributary branches in the thorax and abdomen.

Although variations of veins are more frequent than those of arteries, they have been much less studied, one reason being that veins are rarely injected with paint for purposes of dissection. Their variations also are of much less surgical importance than those of arteries. When arteries are anomalous, so are their accompanying veins; an exception to this rule is seen in the obturator vein which empties into the internal iliac vein, even when the artery is abnormal.

Abnormal communications by aberrant vessels are much more common in the venous than in the arterial system. Many veins which are normal in the lower animals occur as anomalies in man. Many varieties which occur in man are really persistent fœtal conditions, and these are permanent conditions in animals lower in the scale. An example of this is seen in the occurrence of a double vena cava, the supernumerary vessel (the left cava) being merely a persistent left duct of Cuvier.

The following account of the anomalies of veins is nec-

essarily incomplete; the reader who is interested in the subject is referred for further information to W. Krause's "Varietäten der Körpervenen" in vol. iii. of Henle's "Anatomie des Menschen," the various articles in the *Journal*

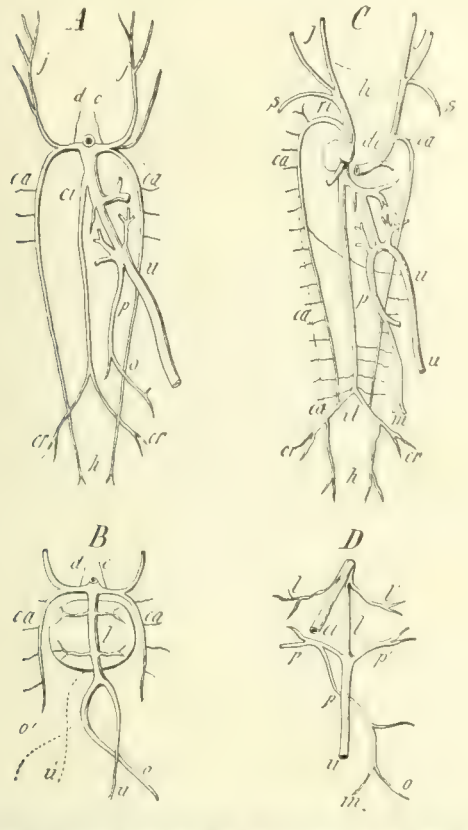

FIG. 4994.—Diagram Illustrating the Development of the Great Veins. (After Kölliker.) *A*, Plan of the principal veins of the fœtus of about four weeks or over, after the first formation of the vessels of the liver and the vena cava inferior; *B*, veins of the liver at a somewhat earlier period; *C*, principal veins of the fœtus at the time of the first establishment of the placental circulation; *D*, veins of the liver at the same period; *dc*, the right and left ducts of Cuvier; *ca*, the right and left cardinal veins; *jj*, jugular veins; *s*, subclavian; *az*, azygos; *u*, umbilical; *o*, omphalo-mesenteric vein; *p*, portal vein; *p' p'*, venæ advehentes: *l*, ductus venosus; *h*, hypogastric or internal iliac veins in the line of continuation of the primitive cardinal veins; *li*, transverse innominate.

of Anatomy and Physiology, and R. Quain's "Commentaries on the Arteries," 1844; and, for an excellent account of the development of the veins, to vol. i., Part I., of Quain's "Anatomy," 1890.

CARDIAC VEINS.—*Coronary Sinus.*—The coronary sinus and the small oblique vein connected with it must be regarded as the persistence of a fœtal condition which will be described in connection with the superior cava; it is really the termination of the left duct of Cuvier, or left superior cava. The vena azygos minor has been seen emptying into the coronary sinus; in this case the left superior cava was persistent as a small branch.

It is not uncommon for one or more of the cardiac veins to be absent. When the left superior cava persists, it may receive veins which normally enter the coronary sinus. The *great coronary vein* may end in the auricle itself, as may also the *middle cardiac vein;* this is the normal condition in the horse, camel, etc.

PULMONARY VEINS.—The pulmonary veins occasionally communicate with other veins, as the innominate (Hyrtl); the right upper pulmonary has been seen to empty into the superior cava, and the left upper into the innominate. The two pulmonary veins of one side may unite into a single trunk (more commonly on the left side) before emptying into the left auricle.

There may be three pulmonary veins on the right side, the third coming from the middle lobe of the right lung. Hepburn[1] records a case of double vena cava in which there were three right pulmonary veins, the upper opening into the superior cava of the right side, and the two lower into the *right* auricle; there was also a separate foramen (quite distinct from the foramen ovale) between the right and left auricles. Peacock[2] records a similar case in a child six years of age.

I have on two occasions seen the upper pulmonary vein of the right side emptying into the superior vena cava. The left vein may open into the innominate. Shepherd[3] reports a case of a single right pulmonary vein opening into the vena azygos major.

DEVELOPMENT OF THE GREAT VEINS.—In order to understand more thoroughly the variations of the great veins which return the blood to the heart, the following description, abridged from Quain's "Anatomy," 9th edition, vol. ii., will be of service:

"At the time of the commencement of the placental circulation two short transverse venous trunks, *ducts of Cuvier*, one on each side, open into the auricle of the heart; each is formed by the union of a superior and an inferior vein named the *primitive jugular* and the *cardinal vein*. The *primitive jugular* receives the blood from the cranial cavity by channels in front of the ear, which are subsequently obliterated; in the greater part of its extent it becomes the external jugular vein, and near its lower end it receives small branches which grow to be the internal jugular and subclavian veins."

The *cardinal veins* are primitive vessels which return the blood from the Wolffian bodies, the vertebral column, and the parietes of the trunk. The inferior cava is a vessel of later development, which opens into the trunk of the umbilical and omphalo-mesenteric veins above the *venæ hepaticæ revehentes* (Fig. 4994).

The iliac veins, which unite to form the inferior cava, communicate with the cardinal veins. The inferior extremities of the cardinal veins are persistent as the internal iliac veins; above the iliac veins the cardinal veins are obliterated in a considerable part of their course; their upper portions then become continuous with two new vessels, the *posterior vertebral veins* of Rathke, which receive the lumbar and intercostal twigs.

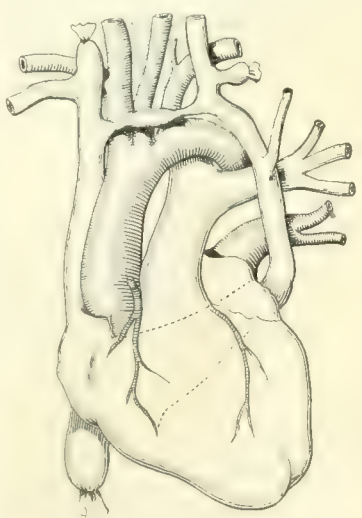

FIG. 4995.—Double Vena Cava seen from the Front, with Small Transverse Innominate Veins. (R. Quain.)

As development proceeds, the direction of the ducts of Cuvier is altered by the descent of the heart to the thoracic region, and then it becomes continuous with that of the primitive jugular veins. A communicating branch makes its appearance between the two jugulars, directed obliquely downward from left to right; further down in the dorsal region, between the posterior vertebral veins, another communicating branch is developed.

The communicating branch between the jugulars is converted into the left innominate vein (see Fig. 4996). The portion of the primitive jugular below the commu-

nicating vein, together with the right duct of Cuvier, forms the superior vena cava, while the cardinal vein opening into it (*az*, Fig. 4994) is the extremity of the great azygos vein. On the left side, the portion of the primitive jugular placed below the communicating branch, and the cardinal and posterior vertebral veins, together with the cross branch between the two posterior vertebral veins, are converted into the left superior intercostal and left superior and inferior azygos veins. The left duct of Cuvier is obliterated, except at its lower end, which always remains pervious as the coronary sinus. Traces of this vein are recognized in the adult as a fibrous band or a small vein (see Fig. 4996, *A*). The variability in the adult arrangement of these vessels depends on the various extent to which the originally continuous vessels are developed or atrophied at one point or another.

Varieties of the Superior Cava and Innominate Veins.—*Double Vena Cava.*—This anomaly is rather a rare one, and is due to the persistence of the left duct of Cuvier. When the left duct of Cuvier persists, the transverse innominate vein is absent or of a very small size, and the vein formed by the junction of the left internal jugular and subclavian is continued down in front of the arch of the aorta and root of the left lung to the heart (see Fig. 4995), where it receives the great cardiac vein, and then passes outward to become continuous with the coronary sinus, and thus opens into the right auricle (see Fig. 4996, *B*).

The explanation of this anomaly is simple, if the description of the development of the great veins, given above, be referred to. It is merely a persistence of the fœtal condition. The left duct of Cuvier is not obliterated, and in consequence the transverse branch between the two primitive jugulars has been developed but slightly or not at all. The persistent left cava has been seen in a few cases to open into the left auricle (Hyrtl, Gruber, and others).

In birds and some mammals, as the rabbit, etc., the left duct of Cuvier persists normally as well as the right.

R. Howden[4] reports a case of double vena cava in which the left vein was joined by a large left azygos vein; the right azygos was broken up into several veins; the most inferior one joined the left azygos, and the superior the vena cava. This is a reversal of the usual condition, and the left azygos in this case must be looked upon as a persistence of the left cardinal vein.

The writer has met with no less than six cases of persistence of the left duct of Cuvier. They all occurred in adults (four males and two females), and were of the

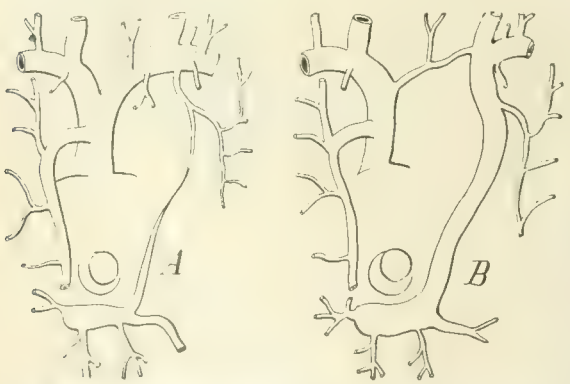

Fig. 4996. *A*, Diagram showing Vestige of the Left Superior Cava with Brachiocephalic, Superior Intercostal, Azygos, and Cardiac Veins. *B*, Diagram showing persistence of left superior cava and its communication with the coronary sinus. (After Marshall.)

usual form; in four the transverse innominate was of considerable size. In the third and fourth cases it was very small, and formed chiefly by the inferior thyroid veins. Instances have been recorded in which the right superior cava was absent and the left persisted; in such cases there was a right transverse innominate vein. This variation occurred without transposition of the arch of the aorta or any of the viscera. In cases of transposition of the viscera this is the normal arrangement.

In some cases the transverse innominate vein is of normal size, and yet there is a persistence of the left duct of Cuvier in its whole length, either as a good-sized canal or as a very small, but patent, vein.

In some cases in which two superior cavæ are present, the left has been seen to enter the left auricle instead of the coronary sinus.

Gruber reports a case in which the principal veins of the heart terminated in a trunk which opened into the left innominate vein, the opening of the coronary sinus into the right auricle being occluded (*Virchow's Archiv*, xcix.).

Connection between the Vena Cava and Pulmonary Veins.—Cases are on record of the upper right pulmonary vein emptying into the superior cava (Meckel, Gegenbauer); of the left pulmonary vein joining the innominate (Bachhammer); and also of the right pulmonary vein opening into the vena azygos major (Shepherd). Hyrtl reports a case in which there was a communication between a rudimentary left cava and the left inferior pulmonary vein.

Transverse Innominate.—This vein may be placed higher up than usual—so high, in fact, that in children with short necks it might be accidentally wounded in the low operation for tracheotomy.

Cooper[5] reports it as passing through the thymus. Gruber examined many embryos of children, and found that in certain cases the vein passed behind the left and in front of the right lobe of the gland, and in others in front of the left and behind the right lobe (quoted by Krause).

Coronary Sinus.—This has been seen to open into the left auricle. Gruber reports a case in which the opening into the right auricle was occluded, and the principal veins of the heart ended in a trunk which passed up to join the left innominate vein.

Vertebral.—This vein not infrequently passes behind the subclavian to reach the innominate, or it may embrace the subclavian by dividing above and reuniting below. It occasionally passes through the transverse process of the seventh cervical vertebra, or sends a branch through the foramen to join the deep cervical vein.

Internal Mammary.—This may be double, and may anastomose with the upper intercostal. The writer has seen it empty into the superior cava. It may empty into the azygos major on the right side (Portal).

Superficial Veins of the Head and Neck.—The arrangement of the superficial veins of the neck often varies greatly from that described in text-books of anatomy.

The two divisions of the *temporo-maxillary* vein are frequently very unequal in size; the branch joining the facial may be of large size, and that going to the external jugular very much diminished, or *vice versa*. In some cases the branch joining the facial returns all the blood into the internal jugular, and in other cases the internal jugular receives no branch from the temporo-maxillary. When the latter arrangement exists all the blood empties into the external jugular.

The *facial vein* sometimes passes back over the sternomastoid muscle to join the external jugular. It may pass across the sternomastoid to its posterior border, and then join the internal jugular beneath that muscle. It sometimes joins the internal jugular behind the posterior belly of the digastric and stylohyoid muscle, or it may be continued downward to the anterior jugular (see Fig. 4998).

External Jugular.—This vein may be double. In those cases in which the posterior division of the temporo-maxillary trunk is wanting, and all the blood goes to the internal jugular, the external jugular is very small, being formed altogether by the posterior auricular.

When the posterior auricular joins the temporo-maxillary trunk, the external jugular is wanting altogether in the upper part of the neck. Gruber describes a case in which a loop was formed in this vein through which passed the transverse cervical nerve. The lower end of

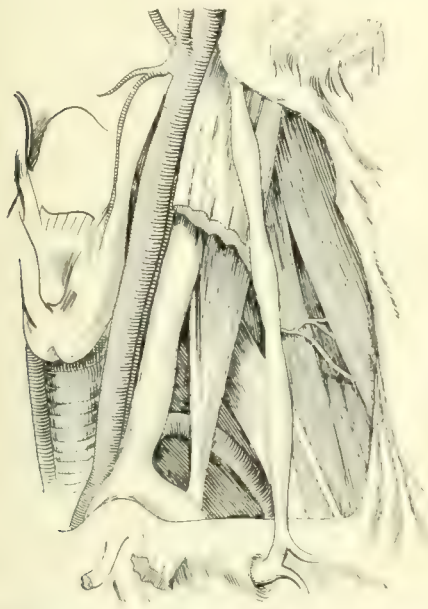

FIG. 4997.—External Jugular passing over the Clavicle and going up between that Bone and the Subclavius Muscle to join the Subclavian. (Richard Quain.)

the external jugular may divide into two branches, one of which joins the subclavian vein or transversus colli, and the other the anterior jugular, subclavian, or internal jugular.

Occasionally the vein may pass over the clavicle and join the cephalic vein, or the cephalic may join the external jugular beneath the clavicle, and communicate with it at the same time by a loop line above the clavicle (Nuhn). (See Fig. 4999.)

The writer has seen several cases in which the external jugular passed over the clavicle and then turned up between that bone and the subclavius muscle to join the subclavian (see Fig. 4997). A knowledge of these anomalies is important in operations on the clavicle and subclavian artery.

According to Hallett, the external jugular is absent once in ninety-three subjects.

Anterior Jugular Veins.—These veins are not constant. One may be much larger than the other. Occasionally the two join to form a single median trunk. The two veins may be united by a large trunk over the trachea, which may give rise to troublesome hemorrhage if wounded in the operation of tracheotomy.

Pilcher says that when one of the veins is absent it is compensated for by a large obliquely transverse branch which comes from the external jugular and crosses the neck at its lower third to join the anterior jugular which persists.[6]

Pilcher also describes a deep anterior jugular of large size which is occasionally seen. It has its origin in the subhyoid region, passes down directly in the median line, deeply seated beneath the muscles; it passes over the cricothyroid space, and, going down the middle of the neck over the trachea, receives the superior and inferior thyroid veins, and finally empties into the transverse innominate vein.

The anterior jugular may in rare cases pass outward over the sternomastoid muscle.

Transverse cervical and suprascapular veins not infrequently empty into the subclavian vein independently. Occasionally they join the internal jugular (R. Quain).

Internal Jugular.—This vein frequently covers the common carotid artery to such an extent that the artery cannot be seen until the vein is drawn aside (see Fig. 4998). According to R. Quain[7] this occurs most frequently in the left side. The left vein is occasionally of very small size, its place being taken by the external jugular (W. Krause). This is a persistence of an early fœtal condition, for in early fœtal life the primitive or external jugular returns all the blood from the heart. This is the normal adult condition in many mammals, as rabbits, squirrels, etc. The internal jugular is altogether absent in fishes, many amphibia, birds, and some mammals, as the horse and ruminants.

A case is reported by J. W. Williams[8] in which the right omohyoid muscle, instead of passing over the vein, "played by means of its intermediary tendon through a slit in the vessel."

In some cases the temporo-facial trunk fails to empty into the internal jugular, the external receiving all its blood.

R. Quain reports a case in which a very large anterior jugular vein communicated with the internal jugular over the carotid artery (see Fig. 4998).

The internal jugular may receive the vertebral, the transverse cervical, and the suprascapular veins. A superior intercostal has been seen to empty into it (Lauth);

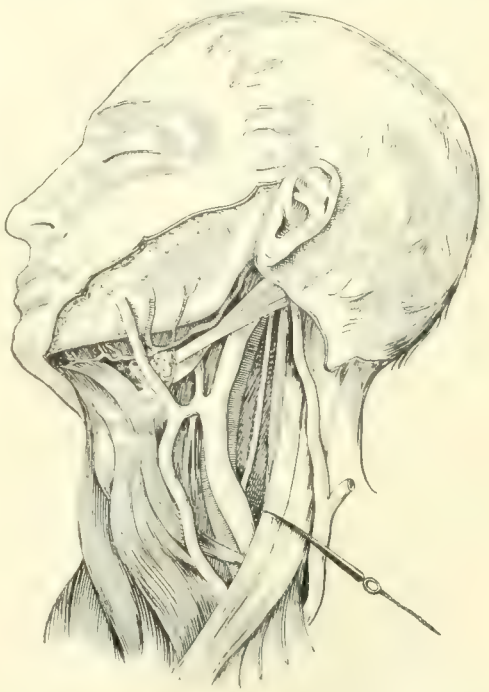

FIG. 4998.—Facial Vein, continuous with the Anterior Jugular, which is Joined to the Internal Jugular by a large Communicating Branch over the Carotid. The internal jugular is seen covering the upper part of the carotid artery. (R. Quain.)

or a large bronchial vein (Weber). The external jugular has been seen to empty into the internal about the middle of the neck (Führer).

VARIETIES OF CEREBRAL SINUSES.*—The sinuses about the *torcular Herophili* are subject to considerable variation. A true confluence of the sinuses is not always found at this point. The torcular may be placed to one side or other of the median line. The connecting branch

*J. F. Knott has given an excellent account of the variations of the sinuses in the Journal of Anatomy and Physiology, vol. xvi.

between the torcular and straight sinus may be of large size and convey the blood from the superior longitudinal sinus.

Superior Longitudinal Sinus.—This sinus may be completely absent (Portal). Knott[9] describes it as being occasionally so small as hardly to represent a normal sinus. It may join the straight sinus; it may bifurcate posteriorly a little behind the coronal suture, and reunite about an inch posteriorly (Knott and Vicq d'Azyr). Malacarne reports a case of bifurcation of the sinus near the apex of the occipital bone, each branch following the lambdoidal suture of its own side and joining the lateral sinus.

Lateral Sinus.—The right is often very diminutive. Lieutaud has recorded a case of complete absence of the left lateral sinus. Both lateral sinuses may be of small size; in such cases the occipital sinuses are much enlarged, and empty their blood into the internal jugular.

Sometimes one or both sinuses are divided into two by a septum (Hallett). Verga describes an aberrant vein going from the cavernous sinus or ophthalmic vein to the left lateral sinus. One sinus may be of large size and the other small. The left is usually the larger. A case is reported[10] in which both lateral sinuses were small, especially the right, which became quite minute after the exit of a large vein through the mastoid foramen. In this case three large emissary veins were present at the anterior extremity of the superior longitudinal sinus, also three others opening into the torcular, one into the commencement of the right lateral sinus, and one into the posterior extremity of the superior longitudinal.

Inferior Longitudinal.—Knott[11] reports a case in which this sinus, instead of joining the straight, turned up between the layers of the falx and ended in the superior longitudinal sinus, one-quarter of an inch above the internal occipital protuberance.

Straight Sinus.—Sometimes absent. In a case reported by Knott the vein of Galen and the inferior longitudinal sinus met at the anterior edge of the tentorium, formed a trunk three-quarters of an inch long, and then divided into three veins, one of which passed up between the layers of the falx to join the superior longitudinal, and the other two passed between the layers of the tentorium to the left side to join the lateral sinus.

Cavernous Sinus.—Complete absence of this sinus is reported by Santorini. There is sometimes a vein from

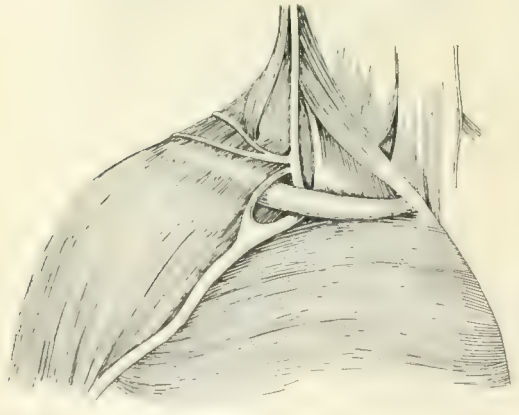

Fig. 4989. Cephalic Vein passing up under the Clavicle to Join the Subclavian. The cephalic is connected with the external jugular by a loop line which passes over the clavicle. (Nuhn.)

it going through the foramen rotundum with the superior maxillary division of the fifth cranial nerve (Nuhn).

Superior Petrosal.—Sometimes absent; may communicate with the ophthalmic vein (Verga).

Inferior Petrosal.—Sometimes terminates within the skull above the margin of the jugular foramen.

Circular Sinus.—May receive the ophthalmic vein.

Occipital Sinuses.—Sometimes wanting, occasionally of large size; in such cases the lateral sinuses are small; they may be very small. The sinus is often much larger than its fellow, and may groove the occipital bone as it passes forward to join the lateral sinus.

Petrosquamous Sinus (Luschka, W. Krause).—This additional sinus is sometimes present, lying in a small groove along the junction of the petrous and squamous portions of the temporal bone, and opening behind into the lateral sinus. In rare cases it is found passing through an aperture (*foramen jugulum spinosum*) in the squamous portion of the temporal bone, between the orifice of the external auditory meatus and the glenoid cavity, and joins the temporal vein. In the dog and many other animals a similar vessel forms the principal outlet for the intracranial blood. In the human subject also, at an early period of fœtal life, the lateral sinus is continued forward in this course, and opens into the primitive (afterward the external) jugular vein; the occurrence of the petrosquamous sinus is due to the persistence of this channel, which usually becomes obliterated after the development of the internal jugular.[12]

Veins of the Upper Limb.—The superficial veins of the forearm are subject to considerable variation, both as to arrangement and as to size. At the bend of the elbow the arrangement varies greatly.

The *radial* vein may be very small or absent, and in such cases the cephalic vein is wanting, the outer branches from the radial side being collected into the median vein, which goes directly to form the *median basilic*. This latter is occasionally double.

The *cephalic* vein may be absent (Hallett found it absent in two out of ninety-three cases). It may be double. It sometimes empties near the insertion of the deltoid into the brachial vein. Sometimes it anastomoses with the brachial vein by an aberrant branch. It may pass up over the clavicle to join the external jugular, or it may be connected with it by a branch called the jugulocephalic (see Fig. 4999). In two cases this branch has been seen to perforate the clavicle (Allen Thompson). This vein may pass up between the clavicle and subclavius muscle to join the subclavian vein; the writer has seen several examples of this anomaly (see Fig. 4999).

The *median cephalic* vein is not infrequently absent.

Basilic Vein.—May be double in its whole course. May anastomose with the ulnar vein. May be separated from the brachial artery by only a very thin fascia; this fact should be kept in mind in bleeding from this vessel. The basilic may anastomose by a large branch with the cephalic vein (Theile).

Axillary Vein.—This vein may be double, from a failure of the venæ comites to unite with the basilic. R. Quain has repeatedly seen the axillary vein perforated by a branch of the internal cutaneous nerve.

Subclavian Vein.—This vein may be placed at a higher level than usual, overlapping the artery at the outer edge of the scalenus anticus. In rare cases the vein passes *behind* the scalenus anticus muscle with the artery, or, in cases in which the artery passes in front of the muscle, the vein may pass behind. Luschka has several times seen the subclavian vein passing between the clavicle and the subclavius muscle. The same anatomist also reports having seen the vein divide and embrace the scalenus anticus muscle, and reunite and follow its usual course. The two venæ comites have been seen to empty into the subclavian; also a left bronchial vein (Weber.)

Double Subclavian.—Morgagni (quoted by R. Quain, p. 182) in one instance found on both sides of the same body two venous trunks placed side by side, instead of the usual single subclavian vein. On the right side the two veins were of equal size, about five inches long, and reached to a point where the internal jugular ends. On the left side one of the veins was of very small size.

The *anterior jugular*, *suprascapular*, or *transverse cervical* may empty into the subclavian separately. Weber reports the subclavian receiving a large bronchial vein. The *cephalic* vein may empty into the subclavian above

or below the clavicle. An aberrant vein may unite the upper end of the cephalic vein with the subclavian by passing behind the clavicular portion of the pectoralis major (W. Krause).

Azygos Veins.—The variations of the azygos veins are considerable, the veins on the left side being especially liable to variation. Two or three of the middle intercostal veins of the left side not uncommonly unite into a single trunk which passes directly into the azygos major. The left superior (hemi-) azygos vein may be absent, the intercostal veins emptying separately into the main trunk. The hemiazygos may empty into the subclavian (Wrisberg) or into the left innominate, joining with the superior intercostal. A case has been reported (Cerutti) in which the hemiazygos joined the internal jugular vein. All the intercostal veins on the left side may be collected into a single trunk which empties into the left innominate, a distribution somewhat similar to that on the right side. The writer has reported an example of this arrangement.[13] By referring to the short account given above of the development of the great veins it will be seen that this anomaly is due to a persistence of the left cardinal vein. A case is recorded by Gruber in which the left azygos opened into the coronary sinus, and was met by a small vein descending from the union of the subclavian and jugular. In this case the jugular vein had been developed in the usual way, while the left vena azygos continued to pour its blood into the left duct of Cuvier (Quain).

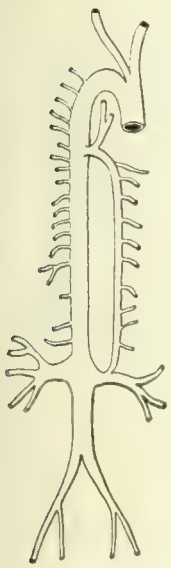

FIG. 5000. The Inferior Cava continued into the Thorax as the Vena Azygos, and the Blood from it Entering the Heart through the Superior Cava. In this case the hepatic veins opened into the right auricle in the usual situation of the inferior cava. (R. Quain.)

The azygos veins may be transposed, the larger vessel being placed on the left side and being joined by the right azygos; the trunk formed by these veins then arches over the root of the right lung and opens into the left coronary sinus (Gruber). This is the normal arrangement in the sheep and some other animals.

R. Howden[14] reports a case of double vena cava in which a single large left azygos, after being joined by some of the right intercostal veins, emptied into the left cava near the coronary sinus. The upper right intercostals formed a trunk which emptied into the right cava.

There may be a single azygos vein ascending in front of the spinal column and receiving the intercostal veins of both sides (Wagner). The azygos major may empty into the right innominate (Meckel) or higher up than usual into the superior cava. Wrisberg has described a case in which the azygos major passed through a canal by grooving the upper lobe of the right lung. Most of the varieties mentioned above may be easily explained by studying the development of the veins, for they are all persistent fœtal conditions. The vena cava inferior has been seen continuous with the azygos major. (See Fig. 5000. This will be more fully described with the vena cava inferior.)

The right spermatic has been noted as emptying into the azygos vein, also the left renal and suprarenal veins (Quain).

An aberrant branch has been seen going from the angle of junction of the left renal and inferior vena cava to the right azygos (W. Krause). The right pulmonary vein has been seen to join the vena azygos major (Shepherd, in *Journal of Anatomy*, vol. xxiv.).

Inferior Vena Cava.—R. Quain[15] divides the peculiarities of this vein into two classes: (*a*) Where the vein has the usual mode of termination in the heart; (*b*) where it terminates in the superior vena cava.

The common iliac veins may not join at the usual place; the left common iliac, after sending a branch across to join the right, may pass up on the left side of the aorta and join the left renal. This is not a very uncommon anomaly, and has been seen several times by the writer. It is sometimes called an example of double vena cava inferior. A case is reported by William Osler[16] of occlusion of the vena cava as it entered the liver. There was in this case a double cava arranged as above described (see Fig. 5001); the circulation was carried on by a large branch from the left renal, which probably joined the splenic.

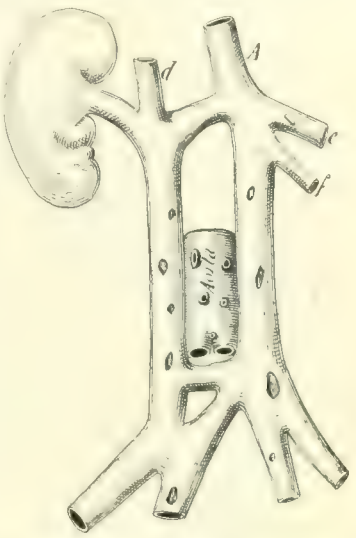

FIG. 5001. Case of Double Inferior Vena Cava, the Two Common Iliacs being Joined by a Transverse Branch. *A*, Occluded vena cava; *e*, right renal; *f*, right spermatic; *d*, large branch, probably joining the splenic, through which circulation was carried on. View taken from behind. (W. Osler.)

In some cases there is no transverse branch below between the two common iliacs (see Fig. 5002). These cases are examples of the persistence of the lower part of the cardinal veins.

Another somewhat similar anomaly is that in which the two common iliac veins join to form a common vein which passes up on the left side of the aorta, but, after receiving the left renal, crosses over (rarely under) the aorta and from there on takes its usual position.

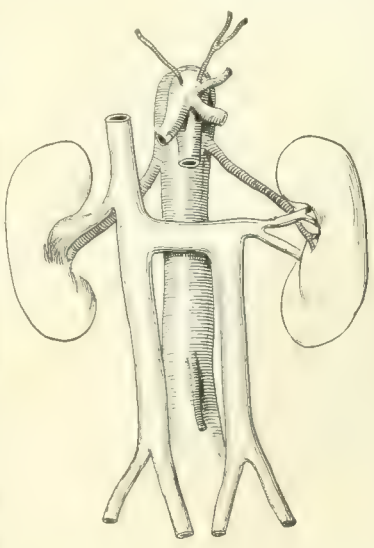

FIG. 5002.—Example of Double Inferior Vena Cava. The left cava is joined by the left renal and then crosses the aorta to join its fellow, and below, the inferior cava proper. Each cava is really a continuation upward of the common iliac vein of that side. (R. Quain.)

The explanation of this anomaly is that the right cardinal vein has been obliterated while the left persists. In cases of transposition of the viscera the vena cava inferior passes up the whole distance on the left side of the aorta, grooves the transposed liver, and joins the right auricle of the heart in its transposed position on the left side. A case of transposition of the viscera is recorded (Hernholdt) in which the inferior cava passed up on the right of the aorta, pierced the diaphragm,

and then crossed over to join the transposed superior cava.

In some rare cases the inferior cava passes up normally to the diaphragm without receiving the hepatic veins, it then pierces the diaphragm, and goes over the root of the right lung to join the superior cava, thus taking the place of the vena azygos major; the hepatic veins in these cases form a trunk, which opens into the right auricle at the usual place of termination of the inferior cava (Fig. 5000). Again, the inferior cava may pass up on the left side of the aorta and, after piercing the diaphragm on that side, go behind the aorta and thoracic duct to join the superior vena cava, thus following the course of the left azygos vein. The hepatic veins, as in the former case, open into the right auricle (see Fig. 5003). These cases are explained on the supposition that the normal inferior cava has never been developed, and that the blood is returned from the lower part of the body by a persistent cardinal vein.

Fig. 5003. Vena Cava to Left Side of Aorta; below, but crossing behind that vessel above, and, passing up the thorax on the right side; it empties its blood into the superior cava. (R. Quain.)

W. Gruber[17] reports a case in which the inferior cava was formed by the junction of three trunks —right and left external iliacs and a common iliac formed by the junction of the two internal iliacs; this arrangement is seen in some of the lower animals, as the bear, etc. The vena cava inferior is occasionally formed by a common iliac vein and the veins of the other side, not opening by a common trunk, but separately.

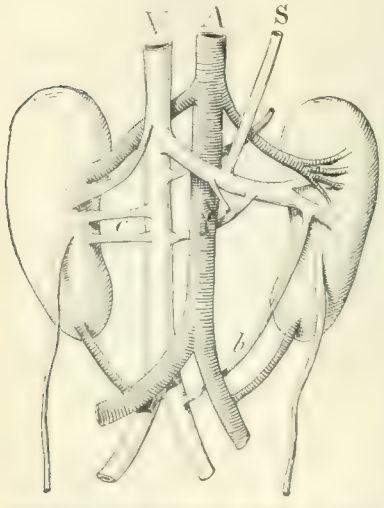

Fig. 5004. Anomalous Renal Vessels. *A*, Aorta; *V*, vena cava; *b*, communication between the left renal and the left common iliac; *S*, vein from left renal going to join the splenic; *c*, supernumerary renal veins. (Shepherd.)

Renal Veins.—The left renal vein, in order to reach the inferior cava, may pass *behind* instead of in front of the aorta. Supernumerary renal veins are not so common as supernumerary renal arteries, but they not infrequently occur. One of these supernumerary vessels of the left side may open into the azygos of that side.

Walsham[18] reports a case of double left renal vein embracing the aorta, one passing in front and the other behind. The posterior branch received the spermatic and also the third lumbar vein. The writer has seen a somewhat similar case, referred to below. When the kidney is placed lower than normal, a vein from it usually empties into the common iliac.

In the museum of McGill University is a beautiful specimen of abnormal renal veins obtained by the writer. Both kidneys were placed lower down than normal, reaching to the intervertebral substance between the fourth and fifth lumbar vertebræ, and each received a supernumerary artery from the common iliac artery. On the right there were two renal veins, on the left one large vein proceeded from the hilus of the kidney in front of the aorta, and a smaller one passed behind the aorta to join the inferior cava lower down. This communicated below, by a large branch which passed beneath the left common iliac artery, with the left common iliac vein, and above, by another large branch, with the splenic vein (see Fig. 5004). This case is probably one of persistence of the left cardinal vein in its lower part.

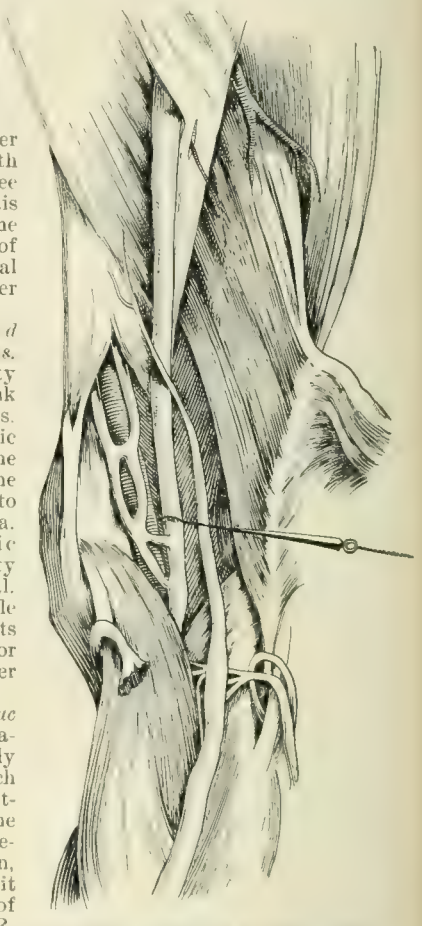

Fig. 5005. Example of Popliteal passing up the Thigh to Join the Profunda. In this case the lower end of the femoral artery is accompanied by a very small vein. (R. Quain.)

Spermatic and Suprarenal Veins.—These may empty by a common trunk into the azygos. The right spermatic may empty into the right renal and the left spermatic into the inferior cava. The spermatic vein may empty into the suprarenal. It may be double in the upper parts of its course or may be altogether absent.

Common Iliac Veins.—A perforation is occasionally seen through which passes a small artery. Sometimes the vein divides and reunites farther on, thus making it double in part of its course (R. Quain). The left common iliac vein has been seen passing in front of the right common iliac artery (Zaaijer). Absence of the common iliac vein of one or both sides has been met with by Gruber; the left external and internal iliac veins in one instance being continued upward to enter the commencement of the inferior cava, and in another the two internal iliac veins were joined into a common trunk which united with the right and left external iliac veins to form the vena cava.[19]

Obturator Vein.—Often double, one accompanying the artery and the other coursing around the inner side of the femoral ring. It may open by two mouths into the external iliac.

Internal iliac vein of the *right* side has been seen to empty into the *left* common iliac vein. The internal iliac may be double (Quain).

Veins of the Lower Limb: Superficial Veins — *External Saphenous.*—This vein may empty into the long saphenous or femoral instead of the popliteal. It may communicate with the gluteal veins beneath the gluteus maximus muscle.

A case is reported[20] in which the external saphenous, after piercing the deep fascia in the popliteal space, ran

Fig. 5006. Case of Double Popliteal Vein. (R. Quain)

up on the posterior surface of the adductor magnus, perforating it near the second perforating artery, and then joined the profunda vein. In the same paper another case is mentioned in which the venæ comites of the posterior tibial, instead of uniting to form the popliteal, continued up as two veins, being joined by the external saphenous, and going up on the adductor magnus to open into the profunda vein near the first perforating artery. The writer has seen the external saphenous empty about the middle of the thigh into an abnormal popliteal vein which passed up the back of the thigh to join the profunda. The external saphenous may empty into muscular branches in the adductor magnus. Branches of communication have been seen between the perforating and ischiatic veins and the external saphenous.

Internal Saphenous Vein.—This vein may pierce the fascia lata higher or lower than usual. It may be doubled, or may form an island. It may receive the superficial epigastric, circumflex iliac, an accessory saphenous, or the external saphenous. It is in some cases very large, and in others of no great size. There is frequently an accessory internal saphenous.

Deep Veins of the Lower Limb.—*Popliteal Vein* — The veins which form the popliteal occasionally unite farther up than usual, so that the lower part of the artery is accompanied by two veins. In some rare cases the vein is double in its entire length. It may be double as high up as the profunda vein. Sometimes the popliteal vein passes up the thigh and joins the profunda; in such cases the external saphenous empties into this vein high up on the thigh. When the popliteal vein does not accompany the artery to become the femoral, a small vein is occasionally seen with the artery (see Fig. 5005).

The popliteal vein may lie deeper and more internal than the artery and next the bone.[21]

Femoral Vein.—Occasionally double in part and, more rarely, in the whole of its course. When double, the femoral artery lies between the two veins (see Fig. 5007). In some cases one of the veins may cross the artery. Small veins are occasionally observed passing over the artery in various directions, sometimes in transverse loops (see Fig. 5008), or obliquely; these transverse branches usually connect various parts of the double vein. The femoral vein may be much diminished in size when the popliteal vein empties into the deep femoral and pierces the adductor magnus at a higher point than usual. In these cases the femoral vein proper first comes in contact with the artery in the groin. R. Quain mentions a case in which he could find no femoral vein accompanying the lower end of the artery; the writer has seen one such case.

Portal System of Veins.—*Hepatic Veins.*—Rothe, a German surgeon, reported many years ago (1787) a case in which one of the large hepatic trunks from the right lobe of the liver terminated, not in the inferior cava or right auricle, but in the base of the right ventricle. Its entrance was guarded by three valves (quoted by W. Krause). In cases in which the inferior cava, as already described, joins the superior cava, the hepatic veins may open separately (Horner) or by a single trunk (Abernethy) into the right auricle. This arrangement is normal in some animals. The writer has described[22] a case in which the vena cava inferior, after piercing the liver and being joined there by a few small hepatic veins (principally from the left side), passed as usual to the dia-

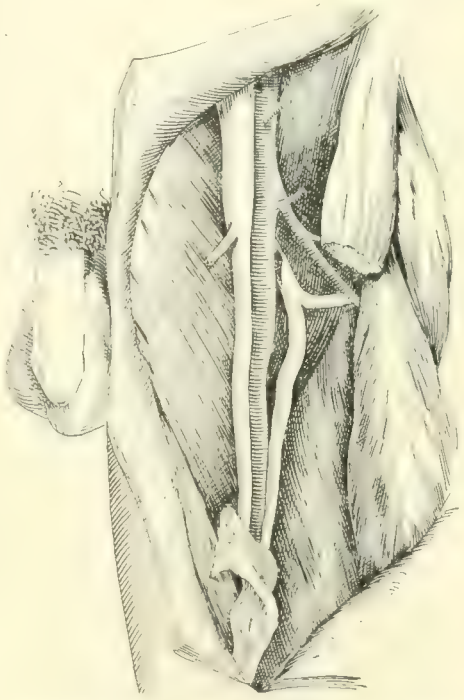

Fig. 5007. Case of Double Femoral Vein. (R. Quain.)

phragm, and as it pierced that muscle it was joined by a large vein, the size of one's finger, and with walls as thick as those of an artery. This vein, when traced back, proved to be a common trunk formed by two large hepatic veins which came from the right lobe; the common trunk measured one inch in length (see Fig. 5009).

Morgagni reports a case of the hepatic veins joining the vena cava inferior after it had pierced the diaphragm (quoted by W. Krause). Hyrtl has seen the hepatic veins empty by a common trunk into the right auricle

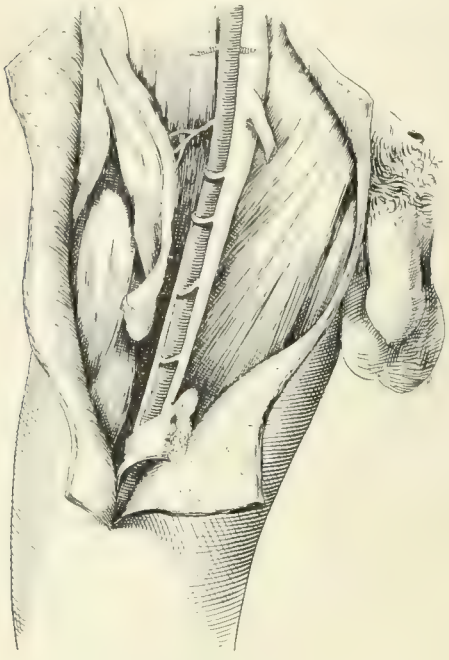

FIG. 5008.—Small Looped Veins passing Over the Femoral Artery, forming a Double Femoral Vein. (R. Quain.)

to the inner side and separately from the inferior cava; this, as mentioned above, is the normal course when the vena cava is absent or its place is taken by a persistent cardinal vein.

Umbilical Vein.—This vein has occasionally been found patent for a variable distance below the liver. It may communicate with the epigastric, and thus establish a collateral circulation; this is much more evident when a diseased condition of the liver obstructs the venous circulation.

J. A. Russel[23] reports two cases of persistent communication between the umbilical and portal veins in the

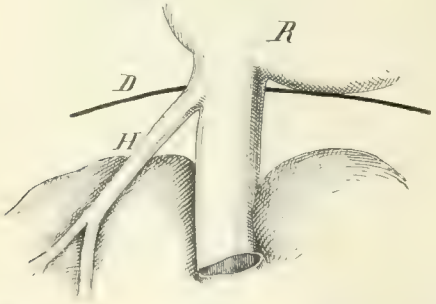

FIG. 5009. Hepatic Veins from Right Lobe of the Liver Opening by a Common Trunk near the Entrance of the Inferior Vena Cava through the Diaphragm. *R*, Right auricle; *D*, line of diaphragm; *L*, liver; *V*, vena cava; *H*, abnormal hepatic veins. (Shepherd.)

human subject. F. Champneys[24] describes a communication between the external iliac and portal veins through the epigastric and umbilical veins.

This was due, probably, to fusion of Luschka's *par-umbilicalis* (which, according to him, always exists normally as a communication between the portal and epigastric veins), and the channel was afterward increased in size by obstruction, due to enlarged liver. A communication of large size between the umbilical and epigastric veins is the normal arrangement in many of the lower animals, as the rorqual, seal, sheep, pig, etc., and in man is an early fœtal condition. Numerous examples have been recorded of communication between the veins of the abdominal parietes, as the phrenic (azygos, etc.) and the portal vein. The writer has already described, in connection with the renal vein, a case in which a large branch of communication existed between the left renal vein and the splenic.

Menière has described a case in which a large vein, as thick as a finger, went from the portal vein to the right iliac. And Brigidi[25] has reported a case of free communication between the umbilical vein, which was patent, and the right iliac by means of a branch of large size in a case of cirrhosis of the liver.

W. Krause[26] mentions a number of cases of communication between the portal vein and the iliac veins by means of a patent umbilical, connected directly by a branch or through an epigastric vein.* These communications are all due to persistent fœtal conditions, and are much more apparent when there is any obstruction to the portal circulation. *Francis J. Shepherd.*

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VEINS, PATHOLOGY OF.—In general, the same pathological processes are found in the veins as in the arteries, though varying in degree and importance in the two sets of vessels, some conditions being more pronounced in the arteries, others in the veins. Thus, for example, inflammatory changes are of much more frequent occurrence in the veins; sclerosis and calcification in the arteries. Thrombosis of veins and thrombophlebitis are among the most common and important of pathological conditions; while, on the other hand, from the nature of things, arterial embolism holds a like important place in pathology. In addition to the pathological processes common to both sets of vessels there is a number of morbid conditions peculiar to the veins, among the most important of which may be mentioned varices and phlebectasias.

ANOMALIES.—*Congenital anomalies* in the number, branching, course, and distribution of veins are very common. They are rarely of clinical importance, though at times causing temporary embarrassment during surgi-

* Sappey is of opinion that all recorded cases of free communication between the umbilical and epigastric veins rest on errors of observation; he holds that the dilated vein is not the umbilical vein, but one of the accessory portal veins. Professor Giacomini is also of the same opinion, saying that the umbilical vein, in its course from the umbilicus to the portal vein, neither gives nor receives any branch normally. Professors Bordoni and Romiti, however, have investigated the subject afresh, and find that the umbilical vein anastomoses with the epigastric, not only in infants a few days old, but in those five and six months of age. In bodies of infants several days or months old they never failed to demonstrate the anastomoses between the branches of the epigastric and umbilical veins by means of Richardson's injecting medium (see London Medical Recorder, July, 1888, p. 274).

cal operations. Congenital dilatations or varices are also of very frequent occurrence. They may vary in size from a slight local increase in the prominence of the veins (*venous nævus*) to extensive dilatations of the superficial veins involving an entire extremity, or the greater portion of the trunk or body. Heredity is an important factor. As a rule the condition does not become especially noticeable until about the age of puberty when there is usually a rapid increase in the degree of the abnormality. The superficial veins alone may be affected, or anomalous communications may exist between these and the deep venous trunks, or the entire venous system of an extremity may be over-developed without a corresponding development of the artery. (See *Veins, Anomalies of.*)

Retrograde Changes.—*Atrophy.*—A thinning of the wall of a vein may result from long-continued overdistention, or from a lessened function, as in the case of an amputation stump. As the result of such thinning of the vessel wall there may follow a dilatation of the lumen, formation of varices, insufficiency or rupture of the valves of the veins, or even rupture of the vessel itself. The atrophy may be confined to one venous system or may be universal. The latter occurs particularly in the case of extreme general venous congestion, as in chronic valvular lesions of the heart. A secondary atrophy of the walls of veins appears also as a frequent accompaniment or sequela of a variety of primary conditions affecting the veins, such as phlebitis, etc. Hypertrophy of the vein wall is usually followed by a secondary thinning, which may be associated with retrograde changes, such as fatty degeneration, hyaline change, calcification, etc. A secondary thinning of the vein wall is also of common occurrence in varices.

Fatty degeneration occurs in the intima of veins under the same conditions as in that of arteries (anæmia, intoxications, infections, etc.). In the intima of the affected vein there are seen whitish or yellowish spots or patches which are usually slightly elevated above the general surface of the intima. The degeneration is usually confined to the endothelium, and the affected cells are more easily scraped from their basement membrane than are the normal cells. In long-continued and severe intoxications, as in sepsis, chronic nephritis, icterus, pernicious anæmia, etc., extensive fatty degeneration may be found in the intima of the veins. Similar marked changes may also be found in very severe cases of certain of the acute infections, such as diphtheria and pneumonia, also in severe anæmia due to hemorrhage, and in poisoning with phosphorus, arsenic, etc.

Hyaline degeneration of the connective tissue of the walls of veins, while not so common as in the walls of arteries, is nevertheless of relatively frequent occurrence. The radicles of the portal vein are most often affected, but the process is common enough in the femoral veins and in the veins of the lower extremities. The spermatic and ovarian veins, and the veins of the broad ligament not infrequently show this change. It may be primary or follow secondarily upon a chronic phlebitis. The change may be diffused or localized. In the majority of cases it is the sequela of a fibroid thickening of the intima, the new connective tissue formed beneath the endothelium soon becoming hyaline in character (phlebosclerosis). Calcification and fatty degeneration may follow, but are much less common than in the case of the arteries. The portal radicles, hepatic veins, and the veins of the lower extremities are most frequently affected. When occurring primarily and not as a sequela of phlebitis, hyaline degeneration of the wall of veins is usually dependent upon a chronic intoxication, as in the case of syphilis. The media and adventitia are rarely involved. After thrombosis of a vein and subsequent organization of the thrombus the newly formed connective tissue replacing the thrombus may become hyaline in character. In extreme chronic passive congestion of the lungs (mitral stenosis) the pulmonary veins as well as the arteries may become greatly thickened and present a hyaline change of greater or less degree.

Calcification.—This is on the whole relatively rare in veins, and is usually localized to small areas. Only rarely are veins calcified throughout any considerable portion of their wall. The deposit of lime salts most frequently follows hyaline or fatty changes, or is a sequela of thrombophlebitis. In cases of chronic phlebitis true bone may sometimes be formed in the walls of veins. This event occurs particularly in the femoral and its branches and in the radicles of the portal vein. The writer has observed a number of cases of calcification of the femoral and saphenous veins following thrombophlebitis of these vessels. In two cases osteoid and true osseous tissues were found in the vein walls and in the adjacent tissues. Calcification of the portal vein is of not infrequent occurrence. Virchow, Spiegelberg, and others have described such cases. The lime salts are deposited in the form of thin laminæ, usually in the media of the vein, but at times also in the intima and adventitia. Evidences of a chronic pylephlebitis are usually present in the form of sclerotic changes, irregular thickenings of the wall, bridges of connective tissue crossing the lumen of the vein, etc. The mesenteric and splenic veins may show similar changes. In two cases of Banti's disease studied by the writer there was a marked stenosis of the portal vein with extensive sclerosis and calcification, involving chiefly the middle coat of the vessel. The irregular character of the vein wall, the roughened intima, and the strands of connective tissue crossing the lumen in one of the cases made it very probable that the stenosis and the accompanying sclerosis and calcification were the sequelæ of an old thrombopylephlebitis. In both cases the splenic and mesenteric veins and their radicles were greatly dilated and showed marked sclerotic changes. Deposits of lime salts were also present in the sclerotic walls of many of the smaller branches of the mesenteric veins. Several similar cases have been reported under various heads in the older literature. In connection with these cases the question arises if the symptom complex now known as splenic anæmia may not be secondary to portal obstruction due to various causes. Sclerosis and deposits of lime salts are not rare in the portal vein and its branches in the late stages of cases of hepatic cirrhosis. Calcification of the vein walls in other parts of the body is of rare occurrence, except in the case of local deposits at the site of calcified thrombi.

Amyloid change is much rarer in the veins than in the arteries, and is usually found in but slight degree. It is extensive only in the case of extreme general amyloidosis.

Progressive Changes.—*Hypertrophy* of all three coats of the vein wall with dilatation of the lumen occurs in athletes and in individuals accustomed to heavy labor. The degree of hypertrophy bears no constant relation to excessive muscular activity, and such an enlargement of the veins may be entirely absent in individuals in whom such conditions are present. It must, therefore, be assumed that some inherent peculiarity in the structure of the vein walls lies at the foundation of such hypertrophy. This view is further supported by the fact that individuals not given to marked muscular activity may also show such a venous hypertrophy. In the latter case the hypertrophy is usually congenital and often inherited, particularly from the paternal side. It is probable that such congenital hypertrophy of the veins is due to a primary weakening of the walls or to a lowered tension in the tissues surrounding the vessels. The loss of the aid given to the venous circulation by muscular activity may also play a part in the production of the condition.

A hypertrophic condition of the veins occurs also in the vessels taking part in the formation of a collateral circulation. In general it may be said that stagnation of the blood-flow in veins leads to a thickening of their walls. A general hypertrophy of the venous system may therefore be the result of a general venous stasis, as in the case of heart lesions without proper compensation. In mitral stenosis there is almost always a marked thickening of the walls of the pulmonary veins, and, in case the right ventricle is not compensating fully for the lesion, a similar thickening of the systemic veins also re-

sults. A local venous stagnation may give rise to a local venous hypertrophy. Such enlargement of the veins and thickening of their walls are frequently seen in the neighborhood of tumors. A secondary atrophy follows sooner or later in all cases.

The increase of thickness may involve all three coats, but often the muscularis is alone hypertrophic. At other times the intima may show the most thickening, and in other cases still the adventitia. In the case of collateral anastomoses, particularly in arterio-venous anastomoses and behind obstructions, the vein wall may show a very marked degree of thickening. In the majority of cases such hypertrophies are in reality connective-tissue hyperplasias due to chronic hyperplastic phlebitis. A true muscular hypertrophy and hyperplasia do occur, however. The new connective tissue formed in the vein wall is usually of the character of scar tissue. Secondary atrophy, contraction and thinning, in association with sclerotic changes, fatty degeneration, calcification, etc., follow the hypertrophy. The hyperplasia of the muscularis in the case of collateral anastomoses is to be regarded as purely compensatory in nature, though often associated with inflammatory changes. In all organs in which there has been for some time a condition of marked chronic congestion the number of large veins appears to be greatly increased. It is due to the fact that the walls of the smaller veins become thickened in proportion to the dilatation of the vessel lumen. In these cases the muscle does not become increased in amount, the thickening of the wall being due to a new formation of connective tissue which later becomes more or less hyaline in character.

Inflammation. Phlebitis.—Inflammation is a much more common occurrence in the veins than in the arteries. Though analogous in structure to the latter, the walls of the veins are thinner and weaker, and their coats less sharply differentiated. For this reason it is hardly possible to separate inflammatory processes of the vein walls into endo-, meso-, and periphlebitis. In the great majority of cases all three coats are coincidently affected, the process extending quickly from the intima to the adventitia, or in the opposite direction, so that the entire vein wall becomes equally involved. A further and more important difference between the arteries and veins is the part played by the latter in inflammations of the tissues. In such conditions the arteries present no recognizable anatomical changes; the veins, on the other hand, present the phenomena of a marginal disposition of the leucocytes and diapedesis of the same. In purulent inflammations the smallest veins may become so involved that the elements of their walls suppurate or show signs of proliferation. Such changes should be included under phlebitis in a broad sense, but the term is usually restricted in its application to inflammatory processes involving the large veins.

According to Köster, phlebitis is to be regarded as a *lymphangitis* of the vein wall, the inflammatory process extending along the lymph spaces and lymph vessels with which the wall is richly supplied. The extension upward along the vein (*ascending phlebitis*) is due to an ascending lymphangitis. The vasa vasorum likewise play an important part in the extension of the process. The connection between peripheral lymphangitis and phlebitis is very close. In the case of infected wounds of the extremities the signs of an ascending lymphangitis precede those of phlebitis, the infection of the vein wall following that of the lymphatics.

In all cases of phlebitis in which the intima of the vein is damaged thrombosis results. The combination of thrombosis with phlebitis is known as *phlebothrombosis*, and is to be regarded as one of the most important features of the process. In the case of hæmatogenous infection (intravascular) the formation of a thrombus may constitute the first step of the process, the inflammation of the vein wall following upon this. In the case of periphlebitis (extravascular infection) the thrombosis follows the extension of the process to the intima. By some writers the term *thrombophlebitis* is applied to the first condition, *phlebothrombosis* to the second. This distinction is not commonly observed, however, and the term thrombophlebitis is used to designate both processes. Thrombosis may be associated with either acute or chronic phlebitis.

Etiology.—The infection of the vein may be either intra- or extravascular. In the first case the infection is either of metastatic or of cryptogenic origin. More frequently the vein is involved by an extension (lymphangitis) from neighboring suppurative processes. Infected wounds (trauma, operation, childbirth, etc.) form the most common causes of phlebitis. The primary infection may be of slight degree, or the infection may take place through uninjured tissues (hair follicle). Phlebitis due to infection following abortion or childbirth is of frequent occurrence. In the majority of the infectious diseases phlebitis occurs often, being due either to the direct action of the specific infectious agent, the intoxication, or to a secondary infection. In smallpox, typhoid fever, influenza, erysipelas, diphtheria, dysentery, scarlatina, pneumonia, and gonorrhœa phlebitis not infrequently occurs. In the milder infections, such as measles, it is a more rare complication. Chronic intoxications, syphilis, gout, alcoholism, etc., are regarded by some writers as causal agents in chronic phlebitis. Obliterating endophlebitis in particular has been ascribed to syphilis. By other writers the existence of a specific rheumatic or gouty (alcoholic) phlebitis is denied. Of the micro-organisms causing phlebitis, the streptococcus, staphylococcus, pneumococcus, gonococcus, typhoid bacillus, and the colon bacillus play the chief rôles.

Varieties.—As mentioned above, it is rarely possible in the acute forms of phlebitis to differentiate endo-, meso-, and periphlebitis. In chronic phlebitis such a classification is often possible, the chronic forms being more often confined to the inner and middle coats. According to the chief characteristics of the inflammatory process, there may be distinguished the following varieties of phlebitis:

Phlebitis.	Acuta (hæmatogenous or extravascular).	1. Exudativa. (*a*) Purulenta. (*b*) Suppurativa.	Phlebothrombosis or thrombophlebitis.
		2. Dissecans.	
		3. Productiva, s. adhæsiva, s. organisatoria.	
		4. Gangrænosa.	
	Chronica (hæmatogenous or extravascular).	1. Hyperplastica.	
		2. Atrophica.	
		3. Obliterans.	

Various other terms have been applied by different authors to designate especial features of given cases: *ascending phlebitis, diffuse phlebitis, universal phlebitis, panphlebitis*, etc. *Phlebitis circumscripta* is also applied to a localized phlebitis, more particularly to areas of localized inflammation in the walls of the cerebral sinuses.

Acute Phlebitis.—The vein wall may be infected from the blood (*hæmatogenous*) or from the tissues (*extravascular*). The latter occurrence is probably the more common.

(*a*) *Extravascular Origin.*—In this case the adventitia is first affected, and the early stages of the process appear as a purulent periphlebitis. The lymphatics and the small veins of the vessel wall become filled with leucocytes, and these may collect in such numbers as to give the process the character of a purulent infiltration of the vein wall (*phlebitis exudativa* or *purulenta*). Œdema and liquefaction of the elements of the wall may also take place as the process increases in severity (*phlebitis suppurativa*). Inasmuch as the connective-tissue sheath of the vein wall is very resistant the exudate collects beneath it and extends along the vessel for some distance, giving rise to other abscesses. In this way the vein may become surrounded by a mantle of pus, which may be so great as to separate the vessel from its neighboring tissues and lead to the complete necrosis of the elements of its wall. The media and intima are usually quickly involved by direct extension and also through the lymphatics and vasa vasorum. Ultimately the entire vessel wall may present a dense purulent infiltration; in some cases only traces of the original tissues of the wall can be made out. The thickness of the wall may become greatly increased,

ten to twelve times as great as normal; and the lumen of the vein may be obstructed or wholly obliterated as the result of the swelling alone. In large veins or in the case of a lesser degree of infiltration the intima may show circumscribed areas of bulging corresponding to the points of greatest infiltration. In addition to the swelling caused by the œdema and cellular exudate, hemorrhages of varying size may occur.

The elastic tissue of the media plays an important part in the extension of the infiltration toward the intima. The advancing exudate pushes the elastic fibres toward the intima, and finally breaks through them at the points of least resistance. The elastica interna remains preserved for the longest time, but finally gives way, and the exudate presses through the point of rupture. Finally, the elastic fibres become involved in the complete dissolution of the vein wall.

The damage to the intima results constantly in thrombosis. The thrombus thus formed may be obturating or parietal; in both cases it serves to prevent further entrance of the exudate into the lumen of the vein. In the formation of the thrombus the elements of the blood circulating through the vein may take part, or, as affirmed by Köster and others, the *intravasation* of red and white cells and fibrinogen-containing exudate from the affected wall into the vessel lumen may aid in the formation of the thrombus, or be alone concerned in its production. The inflammation of the vessel wall is, therefore, the primary process, the thrombosis the secondary, the entire process being regarded as analogous to the formation of exudates upon serous membranes, the exudate containing red blood cells, blood plates, leucocytes, fibrinogen, etc., these being poured out from the vasa vasorum over the intima of the affected portion of the vessel. With the formation of the thrombus upon the intima the process may be appropriately designated phlebothrombosis (*phlebothrombosis purulenta*). By Hunter it was termed *phlebitis pseudomembranacea*. By the majority of writers no distinction is made between thrombophlebitis and phlebothrombosis, but by others the distinction as given above is favored. Inasmuch as the thrombosis is in one case the primary process and in the other a secondary, it would seem well to retain the distinction.

The œdema and infiltration of the coats of the affected vein may lead to their separation from each other (*phlebitis dissecans*). In the case of an involvement of a vein in a gangrenous process the phlebitis may also assume a

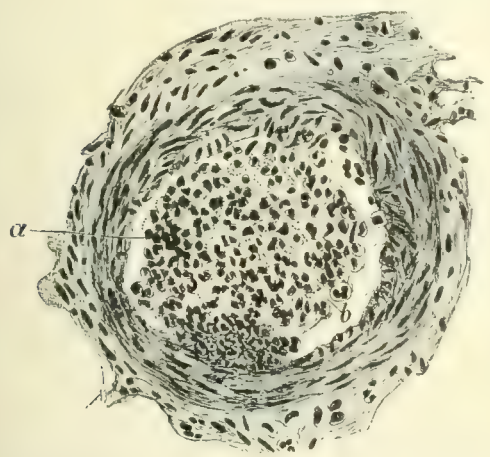

FIG. 5010. Secondary Vasculitis of a Small Vein of the Leg in Phlegmon due to Streptococcus pyogenes. *a*, Leucocytes; *b*, Streptococci. (After Weichselbaum.)

gangrenous character (*phlebitis gangrænosa*). With the advent of thrombosis and the partial or complete obturation of the vessel on the one hand and the cessation of the inflammation on the other, organization of the thrombus may take place (*phlebitis productiva, s. adhasiva, s. organisatoria*) and healing may result. The sequelæ of such healing may be thickening of the vessel wall, obliteration of the lumen, formation of connective-tissue bridges, calcification, etc. During the healing process or subsequently thereto a regeneration of elastic fibres may take place, and newly formed fibres may also be found in the organized thrombus.

(b) Hæmatogenous Origin.—The phlebitis caused by intravascular excitants of inflammation runs a different course. There is usually a primary thrombosis followed by a secondary inflammation. As a result of changes produced in the intima of the vein by toxins, or by the direct action of bacteria, or by the direct action of heat, freezing, trauma, etc., there results a thrombosis. If micro-organisms capable of exciting suppuration are not present in the thrombus (so-called benign thrombus), the only effect upon the vein wall is the slight reactive inflammation caused by the presence of a foreign body. Organization of the thrombus takes place, and it is replaced by newly formed connective tissue and blood-vessels (*phlebitis productiva, s. adhasiva, s. organisatoria*). The sequelæ of calcification, obliteration of the lumen by connective tissue, thickening of the vessel wall, formation of connective-tissue bridges, etc., likewise occur in this connection. Irregular dilatations and stenoses of the affected vein result; the newly formed connective tissue in its lumen may become channelled by new vessels, and the circulation partly or wholly re-established. As the result of such changes the vein may come to have a structure suggesting that of the longitudinal sinus of the dura mater. (Fig. 5011.)

FIG. 5011. Changes Produced in the Inferior Vena Cava and Iliac Veins by the Organization and Contraction of a Thrombus Resulting from the Involvement of the Vessels by a Retroperitoneal Abscess. The irregularities of the intima and the connective-tissue bridges crossing the lumen cause the vessel to resemble the superior longitudinal sinus. (After Schrotter.)

Much more unfavorable is the course if the original thrombus contains pyogenic micro-organisms capable of multiplication. These exert their characteristic effects upon the intima and upon the elements of the thrombus; necrosis, liquefaction, and infiltration of the vein wall follow, the process extending outward toward the adventitia (*thrombophlebitis purulenta s. suppurativa*). The infection of the lymphatics and blood-vessels of the vein wall leads to a further extension of the process, and the surrounding tissues become secondarily involved. The thrombus and the entire vein wall at the seat of infection may be completely destroyed by the suppurative process. Healing and organization may take place; but in the majority of cases the softening of the thrombus leads to embolism of infected material, and the suppurative process repeats itself at the site of lodgment of the emboli.

The presence of pyogenic organisms in the circulation leads to a general pyæmia which is frequently fatal. In the pre-aseptic days this form of phlebitis was much more common than the secondary phlebothrombosis, but it is now relatively more rare. Childbirth, abortion, infected wounds from trauma or operation, malignant endocarditis, acute infections, and secondary infections following the acute infectious diseases are most often followed by hæmatogenous phlebitis. Cryptogenic infections are also common. In the case of infection by certain organisms the phlebitis may assume a gangrenous character (*thrombophlebitis gangrænosa*). This is more rare than in the case of an infection of the vein from the tissues.

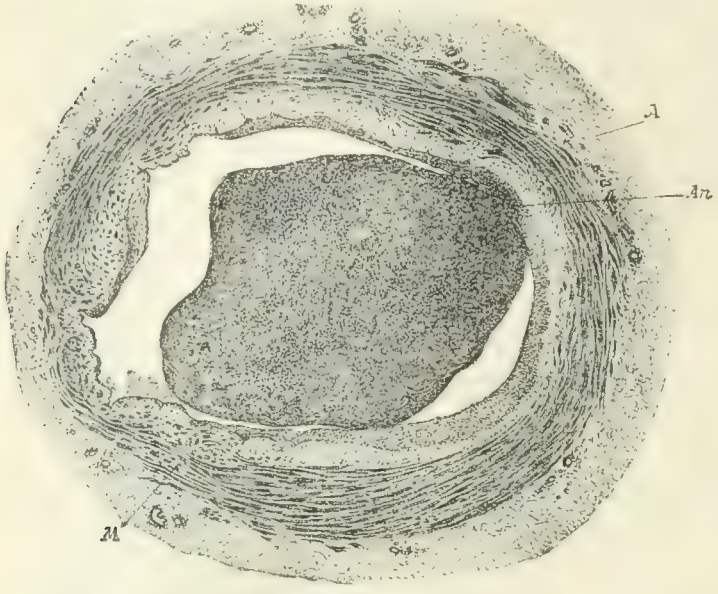

FIG. 5012. Chronic Phlebitis, with Beginning Organization of the Thrombus. *A*, Adventitia; *M*, Media; *An*, thickened intima at point of attachment of organizing thrombus. (After Schrötter.)

Should organization of the thrombus and healing of the phlebitis occur the process assumes the character of a *thrombophlebitis organisatoria*. An *acute productive phlebitis* (*phlebitis prolifera*) without thrombosis may be associated with inflammatory processes in the neighborhood of the affected vessel, as shown by a fibroblastic thickening of the vein wall, dilatation, and thickening of the vasa vasorum, etc. It is also possible that similar changes may be of hæmatogenous origin.

Chronic Phlebitis.—The processes of organization, repair, etc., following an acute phlebitis are often regarded as of the nature of a chronic phlebitis. They are more properly sequelæ. A true chronic phlebitis, however, occurs as the result of chronic inflammations in the neighborhood of veins, and possibly also as a result of chronic intoxications. In hepatic cirrhosis the branches of the hepatic veins usually show chronic inflammatory changes. The veins in the neighborhood of chronic ulcers or abscesses, chronic tuberculous or actinomycotic foci usually show marked changes of the nature of a chronic inflammation. These are characterized by a connective-tissue thickening of the vein wall (*phlebitis hyperplastica*), enlargement of the vasa vasorum, and thickening of their walls, and either a dilatation or stenosis of the vessel lumen. The thickening of the vessel wall may depend to some extent upon a chronic infiltration. Secondary thinning of the wall frequently follows (*phlebitis atrophica*). By many writers varices are regarded as a sequela of chronic phlebitis. Sclerotic changes or calcification may also occur. Thrombosis may or may not be associated with the process. The organization of the thrombus or the proliferation of the intima may lead to an obliteration of the vein at the affected point (*phlebitis obliterans*). (Fig. 5012.)

An *endophlebitis obliterans* (*endophlebitis prolifera*) occurs coincidently with or under the same conditions as endarteritis obliterans. As a result of the proliferation of the intima the lumen is partially or completely filled with a newly formed connective tissue, often resembling myxomatous tissue, and containing numerous new blood-vessels, giving it a certain amount of vascularization. In the majority of cases the condition may be ascribed to syphilis, but similar changes may follow the ligation of veins, thrombosis, and possibly various chronic intoxications. The veins of the lower extremities, the portal radicles, and the branches of the hepatic veins appear to be the most frequently affected. In three cases described by Chiari the proliferation of the intima of the hepatic veins led to a marked stenosis of their lumen, in some vessels even to a complete obliteration, as a result of which secondary changes occurred in the liver, accompanied by overdistention of the portal vein and ascites. Death took place from thrombosis of the obstructed veins. Chiari regarded syphilis as the most probable causal factor in these cases.

Symptoms.—Phlebitis may occur without any individual signs or symptoms; or these may be obscured by the general symptoms of the primary disease. Particularly in the case of the deeply lying veins may symptoms be absent, and the condition may become evident only through the occurrence of thrombosis or of other sequelæ. In acute phlebitis there is usually an irregular fever, which at times may reach a high degree. The course of the vein, if superficial, may be revealed by the presence of a dark blue, or reddish, thick cord, which is very tender on pressure. In the event of thrombosis the cord becomes more firm and hard. If the surrounding tissues are markedly œdematous and infiltrated it may not be possible to feel the vein. Pressure over deep-seated veins is also painful. The pain is also spontaneous, not only along the course of the vein, but also in its neighborhood. An œdematous swelling of the vein or of the tissues surrounding a vein does not necessarily indicate a phlebitis, as the condition may result from a non-infected thrombus. The distention of the superficial veins may in both cases be regarded as evidence of the establishment of a collateral circulation. The symptoms of chronic phlebitis are in general similar to those of the acute, but are less severe. Acute exacerbations are common in the infected cases, the symptoms being those of an acute phlebitis. In the case of superficial vessels the thickening remains permanent, while the redness and tenderness disappear. The development of the collateral circulation is usually more pronounced, and the distention of the superficial vessels lasting in the case of chronic phlebitis.

It must be noted, however, that the symptoms of phlebitis may vary greatly in different cases, according to the cause, location, sequelæ, and the nature of the general or local disease with which it is usually associated.

Diagnosis.—From the above it is clear that the diagnosis of phlebitis is often not possible, the condition being completely concealed under the symptoms of the primary or accompanying disease, the two forming a symptom complex usually designated as *cryptogenic septicopyæmia*. The diagnosis is, however, easy in many cases, particularly when superficial veins are involved. The differentiation between phlebitis with secondary thrombosis (phlebothrombosis) and thrombosis with secondary phlebitis (thrombophlebitis) is in the majority of cases impossible. Neither the nature of the primary affection, the character of the fever or pain, nor the late appearance

of the symptoms in the course of another disease can be used as differential points. Both thrombosis and phlebitis may occur late in an infectious disease, even during convalescence. The persistence in the body of virulent bacteria may lead to phlebitis and thrombosis long after the original attack of the disease.

Occurrence.—The veins of the lower extremities are most frequently affected. The reasons for this are largely anatomical, these veins being more likely to suffer from stasis and consequent dilatations. Trauma with infection is also of frequent occurrence in this region. Varicose ulcers of the legs very often lead to phlebitis of the *saphenous veins*. The *venæ spermaticæ* and *uterinæ* may become infected after abortion or childbirth. Retention of the placenta leads frequently to an infection of the *uterine veins*. The thrombophlebitis beginning in these vessels may extend to the *vena cava* or the *femoral vein* (phlegmasia alba dolens). The *femoral vein* itself is very often affected primarily in the acute infections and in marasmic conditions. Phlebitis of the *hæmorrhoidal* and *vesical veins* follows cystitis, prostatitis, gonorrhœal infections, rectal and perirectal abscesses. Infection through hemorrhoids themselves is also common. In all of these cases the colon bacillus doubtless plays an important rôle. Phlebitis of the *mesenteric veins* and *pylephlebitis* occur in connection withdy sentery, perityphlitis, and other inflammatory conditions of the intestines. In infections of the umbilical cord in the new-born the *umbilical vein* usually presents the picture of a thrombophlebitis purulenta which may extend into the vessels of the liver and into the portal veins. The *veins of the upper extremities* are less frequently the seat of a phlebitis, but show the condition often enough. Infected wounds of the hands and boils are the most common sources of infection. Cryptogenic infection through an uninjured hair follicle may take place. Venesection was formerly the most common cause of phlebitis of the upper extremities. The *meningeal veins, sinuses,* and the *veins of the diploë* are very frequently the seat of phlebitis. Infected wounds of the head, mastoid or middle-ear disease, caries of the petrous bone, etc., give rise to thrombophlebitis of these vessels and further to meningitis and encephalitis. The *internal jugular* may ultimately be affected. The *sinus sigmoideus* plays an important rôle in the extension of infections from the ear. Phlebitis of the meningeal veins and sinus thrombosis may also follow infections through the orbital or nasal cavities. In rare cases carious teeth may be the primary lesion from which sinus thrombosis ultimately results. Phlebitis of the *pulmonary veins* may result from septic infarcts, abscesses, gangrene, and other inflammatory conditions of the lungs. In osteomyelitis the *veins of the bone marrow* present the picture of thrombophlebitis.

Sequelæ.—The most favorable sequela of thrombophlebitis or phlebothrombosis is the organization of the thrombus and the partial or complete obliteration of the affected vessel with the development of an adequate collateral circulation. Embolism of infective material from the primary focus in purulent phlebitis is the most unfavorable sequela. Such an embolism may be direct, retrograde, or paradoxical. In general, it may be assumed that from every phlebitic focus portions of material are set free into the venous circulation. If these contain pyogenic bacteria the emboli given off may cause an endocarditis of the right side of the heart, septic infarcts and abscesses of the lungs; or they may pass through the pulmonary capillaries and give rise to a mitral or an aortic endocarditis, or to pyæmic abscesses throughout the arterial system. Phlebitis in the regions tributary to the superior vena cava may give rise to liver infarcts and abscesses through retrograde embolism. Phlebitis of the pulmonary veins in particular leads to the production of embolic infarcts and abscesses throughout the general circulation, especially of the brain, spleen, and kidneys. Pylephlebitis may lead to infarcts and abscesses of the liver and lungs. In general the sequelæ of thrombophlebitis depend upon the location of the vein, the character and extent of the thrombosis, the presence of bacteria and the variety of the same, the possibilities of embolism, and the vital importance of the affected organs.

Prognosis.—This depends upon the size and location of the affected vein, the bland or infectious nature of the process, the occurrence of embolism, and the importance of the affected organ. In the less severe cases of phlebitis of the lower extremities the prognosis is relatively favorable, even in the case of pulmonary embolism, since the emboli are likely to be of small size. The more severe cases with marked œdema of the extremity (*phlegmasia alba dolens*), in which the principal veins are affected, are very dangerous because of the possibility of emboli of large size or the growth of the thrombus into the vena cava. Sudden death from pulmonary embolism may occur. The etiological factors in phebitis of the larger veins are in themselves of grave significance. The prognosis in the septic cases is always grave because of the possibility of embolism and the occurrence of general pyæmia and septicæmia. The persistence of fever is the most important indication to be followed. As long as there is a daily rise of temperature the danger of fresh thrombosis and embolism or of an extension of the phlebitis is present.

Treatment.—The old methods of treatment with mercurial ointments, iodine, etc., have been entirely abandoned. The local massage employed in their administration made their application a source of danger.

Prophylaxis is of prime importance. Asepsis or antisepsis at all times is the chief means by which the complication of phlebitis and its attendant thrombosis may be avoided. A small boil or even the slightest infected scratch may lead to a dangerous phlebitis. The pernicious habit of "paring corns" with domestic instruments is also a source of infection, which may sometimes run a dangerous and fatal course. The puerperium is obviously a time when modern aseptic precautions should be carefully observed. Abortion with retention of placental fragments is likewise of the greatest danger. Infection through carious teeth should be avoided by prompt attention to the condition. Mastoid and middle-ear disease should receive proper operative treatment. As a result of modern prophylactic measures the dictum of Cruveilhier that "la phlébite domine toute la pathologie" no longer applies. With the almost universal adoption of aseptic and antiseptic measures, pyæmia and puerperal sepsis have become much less frequent, and thrombophlebitis in consequence is a much more rare complication.

In the case of an established thrombophlebitis the most important indication is the avoidance of embolism by means of absolute rest until no doubt exists as to the subsidence of the process and the complete organization of the thrombus, and the establishment of the collateral circulation. This is particularly the case in thrombophlebitis of the extremities, especially the lower ones. Elevation and fixation of the affected limb may be of service in promoting the return flow from the obstructed area. In the event of severe pain the application of cold, etc., may be useful. The dangers of embolism and the results of moving the limb should be thoroughly impressed upon the patient.

Many cases of phlebitis are now treated surgically. The opening and drainage of periphlebitic abscesses should be carried out as soon as possible. Ligation of the efferent veins, exposure of the affected vein with direct antiseptic treatment of the same, or resection of the diseased portion, etc., are recent operations performed with great success. In the case of mastoid and middle-ear disease with extension to the meninges and sinus thrombosis the jugular may be ligated. As the result of these operations the duration of the process is shortened, the dangers of embolism are removed, and recurrences rendered impossible. The more severe the case the greater the indications for such operative interference.

The local and general conditions should receive appropriate treatment also. Septic and pyæmic conditions should be treated according to the conditions.

Wounds of Veins.—*Ruptures, lacerations, bruises,* and *erosions* of veins are of common occurrence. They take place much more frequently in the case of small veins than in the case of the arteries. Aside from direct trauma, an increase of intravenous pressure plays the most important part in the rupture of veins. Hemorrhage from the conjunctival veins may result from spasmodic coughing and vomiting. The same cause may lead to rupture of small veins in the mucosa of the larynx and trachea. The veins of a collateral circulation frequently burst, particularly in the case of œsophageal varices in hepatic cirrhosis. The pressure of a tumor or aneurism upon the great cervical veins may lead to a rupture of the meningeal veins. Ruptures of the veins of the lower extremities are of frequent occurrence. Increase of pressure, fatty degeneration of the vein wall, etc., are causal factors. Rupture of varices and hemorrhoids occurs very frequently. Intense cramps of the muscles of the calf may cause the rupture of small veins. In a case reported by Frerichs fatty degeneration of the wall of the portal vein led to the rupture of this vessel. Rupture of the superior and inferior venæ cavæ may be caused by falls, crushing of the body, etc. A fall upon the head may cause a rupture of a cerebral sinus even without external signs of injury. Bullet wounds of all kinds may occur in the veins in any part of the body. The wound may be caused by the direct action of the projectile or by pieces of bone. Cases have been reported in which the bullet remained embedded in the vein wall.

The sequelæ of such injuries are hemorrrhage into the tissues or body cavities (hæmothorax, hæmatopericardium, etc.), hæmatoma formation, thrombosis at the point of injury, healing, and the formation of a collateral circulation. If the artery is injured at the same time with the vein an *anastomosis arterio-venosa* may be formed. Embolism of air or of portions of the thrombus may also follow. The aspiration of air into the veins is particularly likely to happen in injuries of the veins of the neck, but is seen more rarely in the case of injuries of the veins of the extremities, uterus, head, and possibly through the veins of the stomach in the case of erosions, ulcerations, etc. Repeated small hemorrhages from hemorrhoids or eroded varices may give rise to the severest grades of anæmia. In the case of the loss of large quantities of blood on a single occasion, death may follow immediately or later, as the result of fatty degeneration of the heart and other organs. In the case of injury of the large veins death usually follows at once from the large amount of blood lost, but even in these cases spontaneous recovery may take place. Surgical interference reduces greatly the mortality in these cases. Ligation of the jugular, innominate, axillary, and femoral veins, as well as of the inferior vena cava, has been successfully performed, and a collateral circulation established. Successful healing has also followed the suturing and resection of the femoral and the vena cava.

The treatment of rupture of veins is chiefly surgical. Compression, clamping, ligaturing, and suturing are resorted to according to the conditions. Even in the case of hemorrhage into the body cavities (pericardium, etc.) the bleeding veins may be found and successfully ligatured. In some cases ligature of the corresponding artery may be necessary to subdue the hemorrhage. The occurrence of after-hemorrhage should always be anticipated. General principles of absolute rest, proper position, etc., should also be applied according to the indications.

Perforation of the veins occurs in the case of aneurism, abscess, tuberculosis, actinomycosis, and new growths. Abscesses of the liver may rupture into the inferior vena cava. Erosions are of importance particularly in the case of the stomach veins; in cirrhosis of the liver, splenic anæmia, stenosis of the portal vein, etc., fatal hemorrhage may follow the erosion of the greatly dilated branches of the coronary or œsophageal veins.

Thrombosis.—Thrombosis of veins is of very common occurrence. In general the causes are: Changes in the vessel wall (phlebitis, intoxications, etc.); changes in the lumen (phlebectasias, varices, obstruction, etc.); changes in the composition of the blood (intoxications, anæmia, cachexia, hydræmia, presence of agents causing coagulation, etc.); changes in the blood current (stagnation, retrograde currents, etc.).

According to their location venous thrombi may be divided into *parietal* and *valvular*. A thrombus completely obstructing the vein is called an *obturating* thrombus. Parietal and valvular thrombi are found particularly in the veins of the extremities; obturating thrombi in the uterine, vesical, and hemorrhoidal veins, in the pampiniform plexus and in the dural sinuses. An *autochthonous* thrombus is one arising at the place in which it is found. A thrombus may, however, originate in the saphenous or the femoral, and growing upward by continued accretions finally reach the right heart. This process is spoken of as a *progressive* or *continued* thrombosis.

According to their structure venous thrombi may be divided into *white, red, mixed,* and *laminated*. The red ones are composed chiefly of red cells, and are formed as the result of the stasis of the venous flow. The white or gray thrombi are composed of blood plates, fibrin, or leucocytes, or contain these elements in varying proportions. They are formed during the circulation of the venous blood, and represent substances which are thrown out of the blood. In the case of alternating rates of current the thrombus may be formed of alternate layers of white and red clot (*laminated thrombus*), or the white and red portions may be mixed in varying proportions.

Venous thrombi may undergo simple, purulent, or gangrenous softening, organization, and calcification, or the elements of the thrombus may be loosened from their attachment to the vein wall and be carried away as emboli. Simple softening without embolism, organization, and calcification are the most favorable terminations of thrombosis; purulent and gangrenous softening the most unfavorable. The last two are due to infection, either hæmatogenous or extravascular. Embolism of portions of the thrombus is of importance according to the size of the transported material, and its origin from a bland or infected thrombus. Bland emboli may, if large enough, cause immediate death through obstruction of the pulmonary artery; when smaller they may obstruct the smaller branches of the pulmonary arteries and cause disturbances of the pulmonary circulation (*hemorrhagic infarction*). The embolism may, however, be without effect if the collateral circulation is adequate, as is usually the case in the normal lung. The production of a hemorrhagic infarct of the lung is therefore dependent upon the size of the embolus and the condition of the pulmonary circulation. If the emboli are infective, metastatic abscesses and gangrenous processes are set up at the point of lodgment. The occurrence of multiple infected emboli gives rise to the picture of pyæmia. The larger infected emboli arising from venous thrombi find lodgment in the pulmonary circulation, but the bacteria arising from such thrombi may pass through the lungs and give rise to pyæmic abscesses in the spleen, kidneys, heart, etc. Fortunately, pyæmia is not to-day such a common condition as it was a generation ago. Thrombophlebitis of the uterine veins after abortion or childbirth is the most common source of pulmonary emboli. The diagnosis, prognosis, and treatment is the same as that discussed under phlebitis. (See also *Thrombosis.*)

Phleboliths.—As the result of the calcification of venous thrombi there arise the so-called *vein stones* or *phleboliths*. They usually lie free in saccular dilatations or in varices. Through rotation the calcified mass becomes rounded and smooth. They are found most frequently in the splenic veins, in the hemorrhoidal, vesical, and pampiniform plexuses. Adherent and partly organized thrombi may undergo calcification and appear as calcified masses in the vein wall.

Air Embolism.—This subject is discussed elsewhere. It is only necessary in this connection to mention general facts. Aspiration of air into the veins occurs particularly in the case of wounds of the veins of the neck and upper extremities, but may take place also through the

veins of the head, uterus, and stomach. Small amounts entering the venous blood are absorbed, but in the case of the aspiration of larger amounts, the air collects in the right ventricle and pulmonary artery, forming a foamy mass which the contractions of the ventricle are unable to drive onward, and death ensues from stoppage of the circulation. Opinions differ as to the amount of air which must be aspirated in order to bring about a fatal termination. It is probable that the amount varies; the fatal termination depending in part at least upon other factors.

Phlebosclerosis.—Sclerosis of the veins is a common process, but does not occur to the same extent or with the same frequency as arteriosclerosis. It may involve the entire venous system, or be confined to certain veins or even to portions of these. We may therefore distinguish a *diffuse*, *local*, and *nodal* phlebosclerosis. The changes are rarely so marked as to be distinguishable with the naked eye as is the case in the arteries. Microscopically the process is characterized by a subendothelial formation of connective tissue, which assumes a hyaline character, but undergoes fatty degeneration and calcification much more rarely than is the case in the arteries. In extreme cases a partial or complete obstruction of the vessel lumen may result. These cases are usually secondary to a chronic obliterating phlebitis. Many writers speak of a *primary* and a *secondary phlebosclerosis*, but such a classification is hardly practical, as it is not possible to differentiate between a sclerosis following a phlebitis and one arising primarily.

In the great majority of cases phlebosclerosis is the result of a previous phlebitis, either acute or chronic. In a certain proportion of cases, however, the hyaline thickening of the vein wall may be of a compensatory nature, the new formation of connective tissue and elastic fibres in the intima and media serving to compensate for a weakening of the vessel through loss of its elasticity. Such a weakening of the wall may be congenital, or acquired as the result of a chronic venous stasis following cardiac and pulmonary affections, chronic intoxications, cachectic conditions, etc. Statistics show that the veins of the lower extremities most frequently show a condition of sclerosis, those of the upper extremities next, the venæ cavæ following next in order. The portal, mesenteric, and splenic veins occasionally present a marked degree of sclerosis, which is sometimes associated with extensive calcification and fatty change. The changes may be so marked as to be plainly visible to the naked eye; the smaller branches of these veins may appear like sclerotic arteries. The condition is probably secondary to an old thrombopylephlebitis, but may be caused by an increase of portal pressure due to hepatic disease or portal stenosis. Chronic intoxication may also play a causal rôle. Such sclerosis of these vessels occurs in splenic anæmia and hepatic cirrhosis. Phlebosclerosis usually bears no relation to arteriosclerosis; the latter may exist in an extreme degree without the occurrence of changes in the veins. On the other hand, extensive phlebosclerosis may be seen involving a large portion of the venous system without corresponding changes in the arteries. Phlebosclerosis presents no recognizable clinical symptoms by which it can be diagnosed with certainty. In the case of the superficial veins the condition may be revealed by the presence of thicker and more rigid vessels. In such cases it is necessary to determine whether these appearances are transitory (phlebitis) or are permanent.

Stenosis and Obstruction of Veins.—The lumen of veins may be narrowed or wholly obstructed by compression from without, by diseased conditions of the vein wall, by anomalies of the vein contents, or by combinations of these factors. On account of the thinness and relatively slight elasticity of the walls of veins, particularly of the large veins, the lumen is easily influenced by pressure from without. Such pressure may be due to tumors, aneurisms, abscesses, inflammatory infiltrations, tuberculous processes, gummata, actinomycotic nodules, etc. The contraction of scar tissue in the neighborhood of a vein may likewise affect its lumen. In exudative phlebitis the thickening of the wall due to the inflammatory infiltration may be so great as partially or completely to obstruct the vessel. Sclerosis, calcification, and the thickening of the wall due to chronic phlebitis, may also lead to stenosis or to obliteration of the lumen. Thrombosis is the most common cause of venous stenosis and obstruction. Parietal thrombi lead to stenosis; obturating thrombi to complete obliteration of the lumen. As the result of the organization of thrombi the lumen of veins may be partly obstructed by diffuse or local thickenings of the wall, by connective-tissue bridges, etc. Phleboliths also cause a more or less complete obstruction of that portion of the vein in which they are found. The invasion of the lumen by sarcoma or carcinoma may also lead to the blocking of a vein by tumor masses growing within the vessel. Combinations of these different factors may also occur.

As the result of such obstruction or stenosis the region tributary to the affected vein becomes hyperæmic or cyanotic if the collateral circulation is not perfectly established. If the obstructed vein is a chief vein and the collateral anastomoses are poorly developed, œdema and effusions into the body cavities result. Hypertrophies, chronic inflammations, hemorrhages, and thrombosis also occur in the area of stagnation. The lowered nutrition and diminished resistance of the tissues in such an area predisposes to the occurrence of gangrene.

Stenosis of the superior vena cava may be caused by aneurisms, tumors of the mediastinum, lungs, thyroid, thymus, cervical glands, tuberculosis and actinomycosis of the bronchial glands, gummata, and scars of old tuberculous, syphilitic, and actinomycotic processes. The condition is revealed by the intense cyanosis and œdema of the head and upper extremities, and by the ectasia of the superficial veins. The innominate, vena azygos, inferior vena cava, common iliac, and femoral veins may also become stenosed or obstructed. In all these cases the diagnosis is dependent upon the location of œdema, cyanosis, hemorrhage, and other symptoms due to venous stagnation. The prognosis is more unfavorable in the case of obstruction of the superior vena cava than of the inferior. Cerebral symptoms soon appear in the former case, and dangerous effusions into the pleural and pericardial sacs may occur. In general the prognosis depends upon the nature of the accompanying condition, the rapidity with which the obstruction takes place, and the possibility of the formation of a collateral circulation. The working capacity of the heart is also an important factor. The treatment must be directed to the causal factor as well as to the condition itself. Tumors, aneurism, etc., must be treated according to the indications. In all cases the strength of the heart must be maintained. Venesection may give temporary relief from cerebral symptoms in obstruction of the superior cava. The treatment in the case of obstruction of the inferior cava is more favorable; rest, proper position of the extremities, bandaging, etc., may add much to the patient's comfort. In the case of portal vein obstruction Talma's operation may be attempted. Through new blood-vessels formed in the adhesions set up between the diaphragm, abdominal wall and the liver, spleen, and omentum, the portal stagnation may be relieved to such an extent that ascites is no longer produced.

Phlebectasias and Varices.—Diffuse dilatations of the veins are known as phlebectasias; local or partial dilatations as varices. Phlebectasias are due to a thinning of the vein wall caused by stretching; inflammatory changes in the wall follow secondarily. Varices are due to primary changes in the wall, usually of the nature of a phlebitis which results in a local weakening of the wall. Phlebectasias are cylindrical, serpentine, or cirsoid; varices are saccular, nodular, or bell-shaped. The different forms may pass into each other. The nodular varices may reach the size of a hen's egg. The walls of ectatic veins are at first thin and atrophic, but after a time there develops a productive phlebitis which leads to a connective-tissue hyperplasia and sclerotic changes

with atrophy of the muscle and elastic fibres. Occasionally the latter become increased. The vasa vasorum are dilated and show greatly thickened walls. The lumen of the vein may finally become partly or wholly obliter-

Fig. 5013. Varices of Veins of Legs in a Man Aged Fifty-four Years, Otherwise Healthy. (After Schrötter.)

ated. In the walls of old phlebectasias there is not infrequently a deposit of lime salts. Large amounts of blood pigment may also be found in the wall as the result of hemorrhages. Thrombosis is of common occurrence in the saccular varices; through the calcification of the thrombi there arise phleboliths. The pressure of varicose portions of a vein when lying close together may lead to a pressure atrophy and confluence of the neighboring parts (*varix anastomoticus*). In this way a tumor-like formation composed of communicating cavernous blood spaces may be formed. In the true varix an increase in the length of the affected veins may sometimes occur. The saccular dilatations offer conditions favorable to thrombosis, and the impregnation of the thrombi with lime salts results in the formation of phleboliths.

The chief etiological factor in the case of both phlebectasias and varices is to be found in a general or local disturbance of the circulation leading to an increase of venous pressure and hindering the return flow of the venous blood. A general venous stasis may be caused by cardiac weakness, valvular lesions, diseases of the lungs leading to an obstruction of the pulmonary circulation, loss of the aid to the venous circulation through the lessening of the negative pressure in the thorax, effects of gravity, etc. A local venous stasis may result from the pressure of an aneurism, tumor, gravid uterus, enlarged lymph glands, or from the obstruction of the vein by a ligature, thrombosis, obliterating phlebitis, intravascular growth of tumor cells, constricting bands of scar tissue, tight belts, garters, bandages, etc.; or through inherent weakness of the vein wall (congenital varix), excessive muscular activity, loss of tension in the tissues surrounding the vein, influence of gravity, etc. Stasis in the portal vein is usually secondary to diseases of the liver. The overloaded rectum in cases of chronic constipation may likewise cause an obstruction to the venous flow in its neighborhood. The influence of gravity is shown particularly in the case of varices of the lower extremities. In individuals who habitually stand upright without adequate muscular movements of the lower limbs, especially in long-limbed individuals, varices of the veins of the leg are of very common occurrence. The saphena magna and its branches are most frequently affected. The aid given to the venous circulation by the intermittent pressure exerted upon the veins by the contractions of the muscles is in such cases but slight; through the influence of gravity the veins become dilated, their valves become relatively insufficient, and the vein walls, unable to support the long column of blood in the vena cava, become stretched. Veins which have been dilated for some time do not regain their old calibre. The valves retain their original size, though an increase in the tissues of the walls is necessary to the enlargement of the lumen. Heredity is a factor of some importance in the etiology of phlebectasias and varices. In just what lies the weakness of the vessel wall is not yet known. The state of the tension of the surrounding tissues is also an important factor.

Phlebectasias are most common in the veins of the hemorrhoidal plexus, the spermatic veins, pampiniform and pudendal plexuses, the utero-vaginal and vesical veins, the tributaries of the portal vein, the veins of the lower extremities, etc. Dilatations are of less frequent occurrence in the veins of the œsophagus, pharynx, meninges, brain, and uterus wall. They are of rare occurrence in the veins of the upper extremities. *Hemorrhoids* are the most frequent form of phlebectasias. The knots and convolutions of dilated veins may lie above the anus (internal hemorrhoids) or project from it (external hemorrhoids). Aside from the general etiological factors mentioned above, hemorrhoids may be caused by catarrhal inflammations of the mucosa of the rectum due to constipation. The extension of the inflammation to the vein walls leads to a dilatation of the lumen and a thinning of the wall. The collateral anastomoses of the hemorrhoidal veins make them subject to the influence of stasis in either the portal system or that of the vena cava. Hepatic cirrhosis is therefore associated with more or less extensive formation of hemorrhoids. The dilatations of the œsophageal veins in cases of portal stasis are also styled hemorrhoids (*œsophageal hemorrhoids*). The dilatations of the veins along the spermatic cord are known as varicocele; those of the veins of the abdominal wall in the neighborhood of the umbilicus in the collateral anastomosis of portal stasis are designated the "*caput Medusæ*." In the development of such a collateral circulation the veins of the œsophagus, the hypogastric, spermatic, inferior epigastric, internal mammary, and intercostal veins, the veins of the kidney capsule, the azygos veins, and the small branches in the suspensory ligament of the liver may become ectatic.

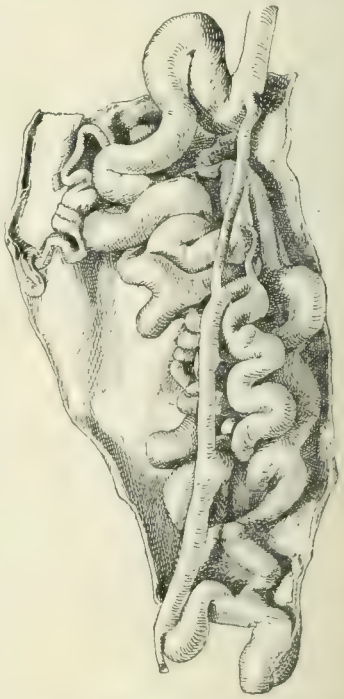

Fig. 5014. Varices from Leg. (After Ziegler.)

The sequelæ of varix formation are of great importance. Rupture of the dilated veins is of common occurrence. This occurs most often in the case of hemorrhoids. Fatal hemorrhage may follow, or as the result of repeated small hemorrhages the most severe types of anæmia may

be produced. Varices of the œsophagus, stomach, and spleen may give rise to fatal hemorrhage or to severe anæmia. Death may follow the rupture of a varix in the brain or meninges. Next to rupture and hemorrhage thrombosis is the most important result of venous dilatation. Embolism from such thrombi is most common in the case of hemorrhoids (after operation) and in the veins of the lower extremities. Thrombophlebitis and lymphangitis are not infrequent complications of varices, and may result fatally. Further, as the result of phlebectasias and the stagnation of the venous flow, the tissues of the region tributary to the affected veins present a condition of chronic œdema. In the case of the skin there

FIG. 5015.—Phlebectasia of Superficial Veins in Case of Obstruction of Venæ Cavæ due to Actinomycosis of Mediastinum. (After Schrötter.)

may be an increased secretion of sweat; in mucous membranes a condition of chronic catarrh results. Hemorrhage by diapedesis from the smaller capillaries is of frequent occurrence. The skin over varices often shows a marked atrophy, pigmentation, desquamation, or a condition of chronic eczema (eczema varicosum). As a result of the chronic venous congestion and chronic œdema the skin is often the seat of a chronic inflammation which leads to a fibroid thickening of the dermis and subcutaneous tissues. Over the legs these thickenings may form irregular folds or nodules (elephantiasis phlebectatica). Ichthyotic thickenings of the stratum corneum may also be produced, the epidermis presenting the appearances of warty excrescences. The neighboring periosteum may likewise be involved in the inflammatory process and a new formation of bone may take place (periostitis ossificans). As the result of slight injuries or wounds torpid ulcers very often form (*ulcera cruris, varicose ulcers*). These run a very chronic course, and may involve a very large part of the skin of the leg. Abscesses of the skin are frequently associated with these. Thrombophlebitis, pyæmia, and amyloid disease may follow such ulcerations.

The diagnosis of varices offers no difficulties. The prognosis is dependent upon the extent of the varices, their etiology, and the occurrence of such complications as thrombophlebitis, embolism, hemorrhage, chronic ulcerations, amyloid disease, etc. The treatment of varices is chiefly palliative: elastic stockings, bandages, etc., ligatures, cauterization, electropuncture, excision, injec-

FIG. 5016. Formation of Collateral Anastomoses Between the Superior and Inferior Epigastric Veins in Obstruction of Inferior Vena Cava. (After Schrötter.)

tions of ergotin, chloral, etc. The injection methods are at present but little used, and are in themselves dangerous. Trendelenburg's double ligature is the operation

FIG. 5017.—Development of Collateral Circulation in Thrombosis of Subclavian Vein. (After Schrötter.)

most frequently carried out. (See *Anus and Rectum. (Surgical.)*; *Varicose Veins*; and *Sexual Organs, Male, Diseases of.*)

TUBERCULOSIS.—Tuberculosis of the veins occurs most frequently in the veins of tuberculous organs, but also

not rarely in the larger veins in the neighborhood of tuberculous lymph glands, etc. In the latter case the infection of the vein wall takes place through direct extension or through the lymphatics. In rare cases primary tuberculosis of the intima of veins may take place through the presence of tubercle bacilli in the circulation. Involvement of the veins from neighboring tuberculous processes is much more frequent in the case of the veins than of the arteries, and is one of the most common modes of dissemination of disease throughout the body. Tuberculosis of the veins presents no individual clinical picture, the symptoms being covered up by those of the primary infection. In miliary tuberculosis of hæmatogenous origin the veins throughout the body show numerous miliary tubercles in their walls, both in the intima and in the media, appearing as small gray or yellow nodules projecting into the lumen of the vessel. The earliest stages of these may appear as small collections of leucocytes or as agglutination thrombi resting upon the intima. Epithelioid proliferation of the cells of the intima occurs later, and finally typical tubercles are formed. In the case of extension from neighboring tuberculous foci the veins come to present the picture of a caseating tuberculous phlebitis.

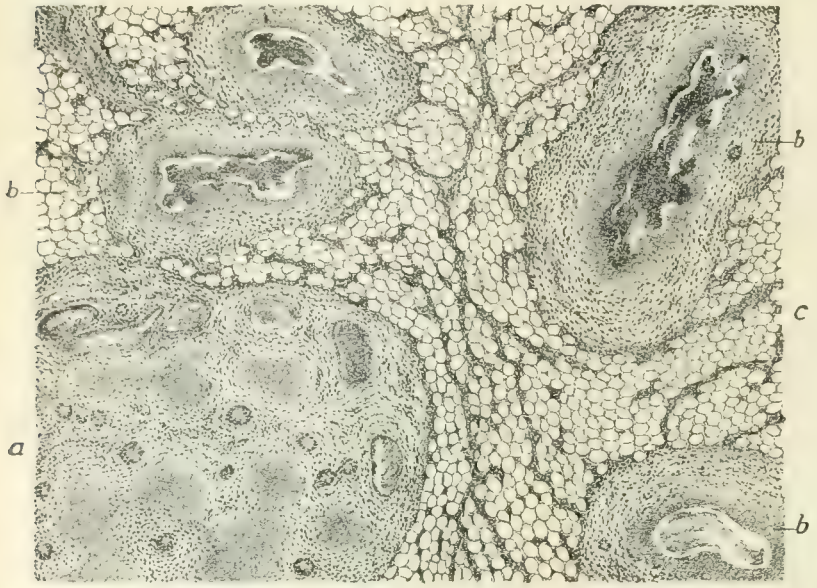

FIG. 5018. *a*, Tuberculous lymph gland with giant cells and caseous foci—large blood-vessels at the periphery; *b*, veins whose walls are thickened by tuberculous granulation tissue, the inner layers of which show caseation; *c*, fat tissue. × 28. (Ziegler.)

SYPHILIS.—The most frequent changes in the veins ascribed to syphilis are of the nature of an obliterating endophlebitis or a chronic periphlebitis. The small veins of the meninges, brain, liver, and other internal organs are most often affected. In the neighborhood of the affected veins there is usually found a gumma or focus of induration. In the great veins, and particularly in the subcutaneous veins, symptoms of an acute phlebitis occur frequently in the early stages of syphilis, as shown by swelling, redness, and tenderness corresponding to the course of the affected vessel. In the later stages gummatous infiltrations of the vein walls and the neighboring tissues also take place. The proliferation and formation of granulation tissue may begin in the intima, media, or adventitia. Thrombosis may be associated with any of these processes. Sclerotic changes, calcification, and fatty change may follow. The portal vein may show marked changes of this character. Chiari has described a proliferating endophlebitis of the hepatic veins which he regarded as of syphilitic origin. Similar changes have also been found in the veins of the intestinal wall and mesentery associated with multiple strictures of syphilitic nature. In congenital syphilis the veins of the umbilical cord may show a thickening of the intima, due to a cellular proliferation or new formation of connective tissue. A peripylephlebitis syphilitica neonatorum has also been described. With the exception of the typical gummata which occur but rarely in the vein walls, the venous changes ascribed to syphilis present no distinctive characteristics, and the syphilitic origin in the majority of cases can be regarded as only probable.

ACTINOMYCOSIS.—The veins in the neighborhood of actinomycotic foci are frequently involved in the process, the resulting changes being of the nature of a chronic purulent phlebitis. Rupture of the focus through the intima may lead to a metastasis of the infection.

LEPROSY.—In lepra nodosa and anæsthetica the veins are frequently affected, presenting nodular thickenings. Microscopically the media and adventitia are infiltrated with round cells, the intima is thickened and hyaline, and the vasa vasorum are thickened. Bacilli are found in all three layers. The process is therefore to be regarded as a bacillary invasion phlebitis.

PARASITES. — Echinococcus cysts of the liver not infrequently break into the hepatic vein and give rise to metastases in the right heart and lungs. The cysticercus, filaria sanguinis hominis, and distoma hæmatobium are also found in the veins.

FOREIGN BODIES.—Under very rare conditions foreign bodies which have entered the veins may be found attached to the wall of the vessel. One case is reported of the finding of a small pistol bullet in the internal jugular.

NEW GROWTHS. — Hæmangiomata, angiosarcomata, and endotheliomata may be primary in veins, particularly the smallest veins. Primary myomata of veins have also been described. Many of the cases reported as primary tumors

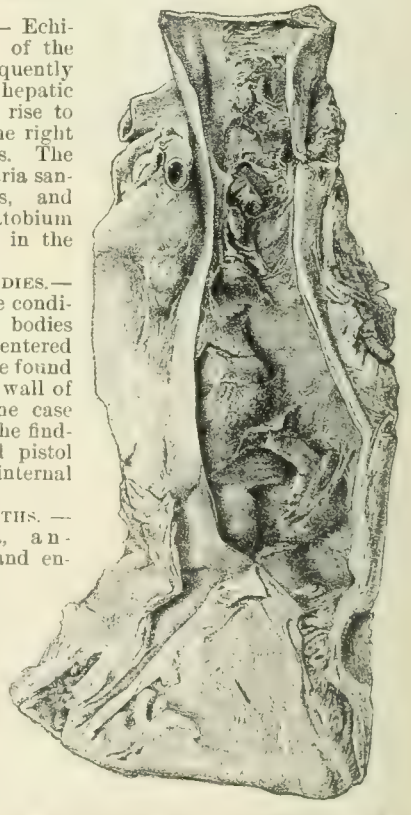

FIG. 5019. Changes in Inferior Vena Cava due to Syphilis. (After Schrötter.)

of veins are of doubtful nature, it being very probable that the vein walls were secondarily involved. In so far as the metastasis of tumors is concerned, the veins play a much more important part than the arteries. The secondary involvement of veins by primary carcinoma and sarcoma of other organs and tissues is of very common occurrence. In the extension of the tumor into the vessel wall rupture of the tumor cells into the lumen is prevented for a long time by the endothelium, which is apparently very resistant to the advancing tumor cells. Large nodules may project into the lumen of the vein, but on microscopical examination the endothelium will be found intact over the growth. Carcinomata break through the walls of large veins more rarely than do sarcomata, because of the plastic influence which the carcinoma cells exert upon the connective-tissue cells of the vessel wall. As the carcinoma cells approach the vein wall the cells of the latter undergo proliferation, and a layer of new tissue is formed between the vein and the tumor. In the case of sarcoma there is but little plastic influence exerted upon the vessel wall, the cells of the tumor being genetically related to those of the vein wall.

In the case of primary malignant tumors of the adrenals, kidneys, testis, etc., large tumor masses not infrequently grow into the veins and may extend into the vena cava. Portions of these may break loose and lodge in the heart or pulmonary arteries. Free tumor emboli may occasionally be found in the right ventricle. Secondary carcinomata of the liver frequently break into the hepatic veins and give rise to metastases in the lungs. In the case of tricuspid insufficiency or violent spasmodic coughing a retrograde transportation of tumor cells may take place (retrograde metastasis). In very vascular tumors the veins are often markedly ectatic.

Aldred Scott Warthin

VENESECTION. See *Blood-letting.*

VENOM. See *Poisonous Reptiles*, and *Toxins, etc.*

VENTILATION. See *Air*, and *House Sanitation.*

VENTNOR, ISLE OF WIGHT.—The Isle of Wight possesses certain favorable climatic features, both on account of its geographical position off the south coast of England, and also on account of its peculiar geological formation. It is at Ventnor, however, on the south side of the island, that the conditions are the most favorable for a winter resort, and Ventnor rivals Bournemouth in its reputation for the climatic treatment of pulmonary tuberculosis, both resorts having a royal national hospital or sanatorium for cases of consumption.

In general, the climate of the Isle of Wight is a marine, moist, mild one, cool in summer and mild in winter, with the prevailing winds from the southwest, *i.e.*, from the ocean. At every season of the year one can obtain here a mild tonic sea air.

In the southern portion of the island a great range of chalk downs stretches from east to west, and in the southeastern portion these downs form high, precipitous cliffs constituting the coast line, broken here and there by "chines" or deep indentations. Between the sea and these high cliffs is a narrow strip of coast-land, called the "Undercliff," consisting of irregular terraces of chalk and sandstone, the results of landslips from the cliffs above. This undercliff is from 100 to 150 feet above sea level, and extends for a distance of about six or seven miles. The aspect of the undercliff is, in general, due south. In the rear, to the north, rise the cliffs, the precipitous face of the downs, which are from 400 to 800 feet high, thus affording complete protection from the northerly winds.

Upon the undercliff, and upon a series of rocky terraces formed by the landslides, Ventnor is built, a town of about 6,000 inhabitants, stretching from the beach up the cliff to a height of nearly 500 feet; consequently the streets are very steep, and among the picturesque features of the place are this precipitous steepness and the arrangement of the streets one above another. Indeed, there are but few level stretches, and those are down by the sea.

The soil consists of soft sandstone and chalk, and is fairly absorbent and dry, but it forms readily, in dry weather, a light irritating dust. The vegetation of the undercliff is exceedingly luxuriant and varied, a proof of the mildness of the climate and the protected situation. Spring opens early, and many plants and shrubs blossom

Fig. 5020. View of Ventnor, Looking Westward.

throughout the winter. "Next to its picturesque situation, the most striking feature of Ventnor is the sea—a great brilliant mirror, reflecting, in fine weather, the light and heat of the sun against the cliff and town" (J. Mitchell Bruce, M.D., "Climates and Baths of Great Britain," 1895). There is a sandy beach affording good bathing, and there are also an esplanade and a pier. Ventnor is well drained by an efficient sewerage system, and is supplied with pure water, though hard from the influence of the chalk. The town is healthy, the death rate being 17.6.

The accompanying chart indicates the various climatic characteristics. In the first place, one observes the great equability of the temperature, not only in the yearly but in the daily range, and the absence of extremes of heat or cold.

CLIMATE OF VENTNOR, ISLE OF WIGHT. LAT. 50° 45' N., LONG. 1° 20' W.

	Jan.	Feb.	March.	May.	July.	Sept.	Nov.	Year.
Temperature (Degrees Fahr.).—								
Average or normal...	41.6°	41.9°	43.1°	53.3°	61 2°	59.1°	47.8°	50.8°
Mean of warmest....	45.7	46.1	48.6	59.6	67.0	64.6	51.9	56 1
Mean of coldest	37 4	37.7	37.6	47.1	55.3	53 7	43.7	45.5
Mean daily range	8.3	8.4	11.0	12.5	11.7	10.9	8.2	10.6
Humidity.								
Av. mean relative....	88	86%	81	77%	79%	80	85	81%
Precipitation.—								
Average in inches ...	2 60	2 0	1.78	1.83	2.41	2.58	3.48	28.13
Weather.—								
Amount of sunshine in hours.....	53.0	76 0	126	200	199	175	51	1658
Mean cloud 9 A.M	6.8	6.6	5.9	5.5	6.1	5.8	6.7	6.1
Days rain fell	16.0	13.0	13	12	14	13	18	164

	Winter.	Spring.	Summer.	Autumn.
Wind (Prevailing Direction).—				
Westerly and south-westerly. (Number of days).....	48	57	73	44
Easterly and south-easterly. (Number of days)	42	35	15	47

The relative humidity is high, as would be expected on the seashore. The rainfall indicates a fairly wet climate, the autumn and winter being the wettest seasons. The winds are strong, and southwesterly gales are prevalent. As the prevailing wind comes from the southwest, it blows mild in winter and cool in summer. Easterly winds are, however, not infrequent, particularly in the late winter and early spring, and are "severe and trying." For England the amount of sunshine is large.

From what has been said above it will be seen that Ventnor possesses many qualities of a valuable health resort. Its situation, its well-drained soil, the mildness of its climate, the influence of the ocean, its excellent sanitary condition, and the opportunities for outdoor exercise, all combine to make it such. The existence of a large consumptive hospital here indicates the usefulness of this resort in the treatment of this disease, and the results which have been obtained are fairly favorable. The place is also recommended for convalescents from acute diseases and operations, for weakly scrofulous children, for persons with laryngeal and bronchial affections, hepatic and renal diseases, for the delicate and aged, for those suffering from atonic and nervous dyspepsia, and for those debilitated from any cause. Those suffering from heart disease will find little opportunity for exercise suited to them on account of the steepness of the streets.

Finally, Ventnor, which has been called "the English Madeira," is a most fascinating seaside resort in summer for the healthy, as the writer can testify to from personal experience. Besides the charm of Ventnor itself, with its wealth of vegetation and the beauty of its ocean view, there are innumerable excursions replete with interest all over the island; the roads are excellent, and the means of conveyance good and cheap. Ventnor is easily and quickly reached from London by way of Portsmouth, thence by a short steamer journey across the Solent, and again by rail from Ryde. The accommodations are of great variety and excellent. *Edward O. Otis.*

VERATRINE.—(*Veratrina*, U. S., B. P.; *Veratrinum* P. G.) A mixture of alkaloids obtained from the seed of *Asagræa officinalis* (Sch. et Ch.) Lindley (fam. *Liliaceæ*).

The bulbous perennial named above, native of Mexico and Central America, was long considered a species of *Veratrum*, whence the alkaloids derived their name. The seeds, which are official in some pharmacopœias, and were formerly so in ours, are called *sabadilla* or, more correctly, *cevadilla* seeds, and are narrowly fusiform, with a flattened membranous top about 1 cm. or less (¼ in.) in length; dark, shining, brown, wrinkled. When powdered, the dust excites violent sneezing. Taste bitter and acrid.

The seeds contain upward of four per cent. of alkaloid, isolated and named *veratrine* by Meissner in 1818, under the supposition that it was a pure alkaloid. It is now known to consist chiefly of two alkaloids, for one of which the name veratrine has been retained, the other being called *veratroïdine*. Several others are supposed to be present, but have not been studied.

The mixed alkaloid is thus described by the Pharmacopœia.

A white or grayish-white, amorphous or semi-crystalline powder, odorless, but causing intense irritation and sneezing when even a minute quantity reaches the nasal mucous membrane; having an acrid taste, and leaving a sensation of tingling and numbness on the tongue; permanent in the air.

Very slightly soluble in cold or hot water; soluble in 3 parts of alcohol at 15° C. (59° F.), and very soluble in boiling alcohol; also soluble in 6 parts of ether, and in 2 parts of chloroform.

When heated to 175° C. (347° F.) veratrine melts, forming a light brown liquid. Upon ignition it is consumed, leaving no residue.

An alcoholic solution of veratrine has an alkaline reaction upon litmus paper.

With nitric acid, veratrine forms a yellow solution.

On triturating veratrine with concentrated sulphuric acid, in a glass mortar, the yellow or orange-red solution exhibits, by reflected light, a greenish fluorescence, which becomes more intense upon the addition of more acid, while the liquid is deep red by transmitted light.

On heating a small portion of veratrine with a few cubic centimetres of hydrochloric acid, the liquid will acquire a deep red color.

The isolated and purified veratrine proper ($C_{32}H_{49}NO_9 + H_2O$) occurs in white crystals, melting at 205° C. and soluble in alcohol and ether. Veratridine is an isomer of veratrine, but is not crystalline.

Veratrine is a most poisonous substance, producing violent vomiting and catharsis, followed by intense cardiac depression and acute gastro-enteritis. In ointments, unless very much diluted, it is also irritating, and not free from the danger of being absorbed. In minute doses it is occasionally given (0.0015 to 0.003 = gr. $\frac{1}{40}$ ad gr. $\frac{1}{20}$) for chronic rheumatism, neuralgia, etc., but is becoming obsolete. Externally, as liniment, ointment, or oleate, it is more frequently, yet still rarely, in this country, used for the same purposes. Most of all, however, it is employed in the above forms for pediculosis, both in man and in animals, for which purpose it is very efficient; yet it is not so safe, and no more certain, than washing the affected surface with kerosene, or a weak ($\frac{1}{200}$) solution of corrosive sublimate.

ADMINISTRATION.—The Pharmacopœia authorizes two convenient preparations: the oleate (*Oleatum Veratrinæ*), which is a two-per-cent. solution in oleic acid, and an ointment (*Unguentum Veratrinæ*) consisting of 4 parts of veratrine, 90 of benzoinated lard, and 6 of olive oil.

Henry H. Rusby.

VERATROL, dimethyl-pyrocatechin, $C_6H_4(OCH_3)_2$, is a clear mobile liquid soluble in alcohol, ether, and the fatty oils. It closely resembles guaiacol (methyl-pyrocatechin), but is more irritating, so that its use is chiefly confined to external application. It has been applied with good results in intercostal neuralgia and epididymitis. Diluted with olive oil it is recommended as an abdominal application in tuberculous peritonitis.

W. A. Bastedo.

VERATRUM. *See Hellebore.*

VERONAL, diethyl-malonyl-urea, $C.(C_2H_5)_2.CO.(CONH)_2$, is a white crystalline powder of faintly bitterish taste, and soluble in 145 parts of cold water and 12 of boiling water.

The hypnotic action of various compounds, such as amylene hydrate and trional, is largely due to the presence of ethyl, so Fischer and von Mering, by the introduction of ethyl groups into various substances, have sought to produce a series of new hypnotics. Of this series the most valuable addition to our sleep-producing armamentarium is veronal. As a pure hypnotic this drug resembles trional, but seems to have greater power. Berent found that even when given in the day-time to walking patients it induced drowsiness and sometimes sleep. Würth treated eighty-four cases of insanity with twenty-one hundred doses averaging 0.5 gm. (gr. viij.) three times a day, and found the drug distinctly sedative in motor and maniacal excitement. Rosenfeld was successful in inducing sleep in hysterical and other nervous patients after bromides, chloral, trional, and warm baths had failed. Tolerance is not readily established, and after the first few nights the dose may be reduced by half. Most clinicians advise not to exceed 1 gm. (gr. xv.) at a dose, but in chronic alcoholism, delirium tremens, dementia, and acute febrile diseases, more has been found necessary. Berent used as much as 3.5 gm. (gr. liij.) without unpleasant after-effects other than heaviness and vertigo. Yet there are numerous reports of heaviness, drowsiness, headache, dizziness, and staggering gait after doses exceeding 1 gm. (gr. xv.). The last-named writer considered 1 gm. (gr. xv.) of veronal the equal of 0.015 gm. (gr. ¼) of morphine as a pure hypnotic. Where there is localized pain the drug has no effect. No noteworthy influence is exerted on digestion, respiration, the heart, or the kidneys. A few cases of skin eruption after prolonged use are reported.

Veronal, then, is a sedative to the nervous system, producing after one-half to two hours a sleep resembling the natural. Patients are easily aroused, but soon fall asleep again; when aroused they are in full possession of their faculties. The dose is 0.5–1 gm. (gr. viij.–xv.) in hot milk or in capsule. Roberts Bartholow recommends the combination of gr. x. of veronal with gr. v. of trional.

W. A. Bastedo.

VERMONT MINERAL SPRINGS.—Windham County, Vermont.

Post-Office.—Newfane. Numerous summer hotels in vicinity.

Access.—Viâ Brattleboro and Whitehall Railroad to Newfane; thence two and one-half miles northeast to springs.

These springs are located in the town of Brookline, fifteen miles north of Brattleboro. The situation is on Putney Heights, half a mile east of the West River and seven hundred feet above the surface. The scenery in the vicinity is very pleasing. The situation of the springs commands a view of parts of three States, and includes many points of great beauty and attractiveness. The carriage drives are numerous and very pleasant. Visitors will find excellent accommodations in several summer hotels in the vicinity. The springs are two in number, but only one of them has been improved. This spring issues from a small crevice in an enormous ledge of rock. The water is always cold, but never freezes as it flows from the spring. The discharge is about thirty-two gallons per hour. The company controlling the spring owns a large tract of land surrounding it, and is thus able to protect the water very thoroughly from surface pollution. It has been recently analyzed by Prof. S. P. Sharples, State Assayer of Massachusetts, with the following result:

One United States gallon contains (solids): Iron sulphate, gr. 1.01; calcium sulphate, gr. 0.64; magnesium sulphate, gr. 0.41; sodium sulphate, gr. 0.93; sodium chloride, gr. 0.05; silica, gr. 0.76. Total, 3.80 grains.

This cannot be termed a powerful mineral water, yet it contains iron in sufficient amount to give it useful properties as a ferruginous tonic. Abundant clinical experience goes to show that it has valuable reconstructive properties. It has been found useful in cases of anæmia and debility, enfeebled digestion, and anorexia, and in functional disorders of the kidneys. Locally it is recommended for insect bites, erysipelas, conjunctivitis, etc. The water is shipped in pint- and quart-bottle cases.

James K. Crook.

VERRUCA.—Verrucæ or warts are cutaneous excrescences which consist essentially of circumscribed hypertrophies of the papillary and epidermal layers of the skin. Their clinical characters are rather diverse. Thus, warts are congenital or acquired; they may appear upon any part of the body at any time of life; they are transitory or persistent, single or multiple; though usually small, they may attain a very considerable volume; in shape they may be rounded, flat, or acuminate, sessile, pedunculated, or filiform; their surface may be smooth, rugous, fissured, cauliflower-like; they are soft or corneous, moist or dry; in color they may present the normal hue of the skin or varying degrees of pigmentation.

The present classification of verruca is not satisfactory owing to the fact that our knowledge of essentially differentiating factors is insufficient. Based upon characters which are largely descriptive, a number of varieties are mentioned by authorities as: *verruca acuminata, acquisita, congenita, filiformis, glabra, perstans, caduca, senilis, digitata, dorsi, manus et pedis, vulgaris,* etc. Although these do not suggest a scientific division, a few of the terms enumerated may be used with advantage in the general consideration of the subject.

Verruca Vulgaris.—This is the type most commonly seen; hence the name. The lesions are hemp-seed- to split-pea-sized, single or multiple, discrete or in groups, rounded or slightly flattened, with a rugous surface which presents to the eye the appearance of numbers of closely set papillæ of variable prominence; these are capped with horny epithelium. The color ranges from skin-pink to a dirty grayish-black. The hands, fingers, and exposed parts are the favorite sites, and young people are far more commonly affected than adults.

Verruca Plana.—This variety is seen typically in the young (verruca plana juvenilis) as small, flat, slightly elevated lesions, of round or polygonal outline, and soft, smooth surface. They may be discrete or several may be merged to form more or less irregular plaques. The general appearance is not unlike that of lichen planus, though the color is more yellow than purple. The forehead, temples, cheeks, chin, and hands are the usual locations.

Verruca Senilis.—This form has been designated by some, erroneously, "verruca plana of the aged." It is sometimes seen upon the backs of individuals advanced in years. The lesions are somewhat irregular in outline, of low elevation, papillomatous, pigmented brown, and often covered with a slightly greasy scale. Verrucæ of this type have been called *seborrhœic warts,* and are prone to undergo cancerous degeneration. Similar verrucæ have been observed upon the hands of workers with the *x*-ray; in these also cancerous changes have been recorded.

Verruca Acuminata.—This type (venereal wart) occurs upon the genitalia and adjacent parts of individuals of both sexes; rarely it is seen elsewhere. Usually an irritant is present in the form of a venereal discharge. The

lesions appear as papillary growths, discrete or grouped to form a cauliflower-like mass. Depending somewhat upon pressure effects they are flat and sessile, or elongated and slender. Their usual location—about the corona glandis in the male, and the labia, introitus vaginæ, and anal region in the female—favors the retention of moisture and the maceration of the lesions; the surface, therefore, is usually bright red, and covered with a secretion which is often very offensive; the practical absence of a cornified layer predisposes to slight hemorrhage, so that this secretion is frequently blood-tinged. These warts may appear in situations which are not moist, in which case there is no secretion, and the horny layer covering them becomes much thickened. Verrucæ acuminatæ are sometimes seen during the later months of pregnancy in women innocent of venereal history; they usually disappear after confinement.

Etiology.—The active causes of acquired verrucæ are not definitely known. It is certain that warts are the result of the local action of irritants, but the essential elements in these irritating agents are not known; nor are the predisposing factors, which render one skin more susceptible than another, fully understood. A microbic origin is surmised for verruca vulgaris and verruca acuminata; the former is undoubtedly mildly contagious, certainly for adjacent skin, and probably for the skin of another; while the latter is well known to be auto-inoculable. Verruca plana is said by Jadassohn to produce its kind and therefore has a specific cause; this is confirmed by an eminent dermatologist who, in a personal communication to the writer, reports having observed an epidemic of verruca plana sweep through a family. The exciting cause of verruca senilis is not known, though the progressive degeneration in the skin undoubtedly serves as a predisposing factor. Of the lesions seen upon the hands of *x*-ray operators the cause is obvious.

Pathology.—Anatomically, verrucæ consist essentially of an increased connective-tissue growth as a basis, to which is added an hypertrophy of the papillæ and the rete mucosæ. These changes are accompanied with an increase in the vascular supply. Often the hypertrophy of the papillæ is more apparent than real, the result of the actual increase in the size of the rete pegs. In most verrucæ the horny layer is hypertrophied, though the keratin transformation is not always complete. In verruca acuminata the horny layer is usually very thin, while the papillæ and rete are greatly increased. In the senile wart columns of epithelioid cells are found within the papillary layer; and throughout all layers (excepting the corneous) a peculiar infiltration of fat is present.

Diagnosis.—While the various forms of verruca are generally recognized without difficulty, it is well to keep in mind certain differentiations. *Lichen planus* has been confused with verruca plana; the former is less often seen upon the face, has a more empurpled color, is scaling and infiltrated, and itches, at times intensely. *Molluscum contagiosum* compared with verruca vulgaris is recognized by its minute punctum and its depressed centre. The lesions of *xanthoma* are distinctly yellow and would scarcely be mistaken for verruca. A distinction is also to be made between verruca acuminata of the sessile type and *syphilitic condyloma;* the latter is the papule of syphilis in moist locations, and as such is rarely papillomatous. *Verruca necrogenica* and *tuberculosis verrucosa cutis* may be recognized by their clinical course and by the histological examination of excised portions of the lesions.

Treatment.—The internal treatment of verruca is of doubtful efficacy. Crocker thinks favorably of the use of magnesium sulphate in small doses, and of dilute nitrohydrochloric acid. Arsenic, so frequently used in skin diseases, is rightly credited with good results in certain varieties, especially verruca plana.

The local treatment contemplates the removal of the lesions by curettage, electrolysis, cauterization, or by the application of substances designed to soften or to stimulate the skin. In many instances the use of the curette is most satisfactory; the scraping does not cause severe pain and the bleeding is usually slight; it is often advantageous to cauterize the oozing base with the silver nitrate crayon. In verrucæ which are very vascular the curette must be used with caution.

The method of removal by electrolysis is especially adapted to pedunculated forms: the base is transfixed with a needle connected with the positive pole of a battery, and a current of one to two milliampères is passed for about one minute; this is repeated several times, the needle being inserted at different angles through the base. The obliteration of the vascular supply thus induced causes the wart to shrivel and eventually to fall.

Of caustics glacial acetic acid and the silver nitrate crayon are the best; the use of chromic acid, acid nitrate of mercury, or potassium hydroxide is not without danger owing to their powerful caustic action. For softening the horny epithelium preliminary to curetting salicylic acid may be used; it may be applied in a solution with alcohol and ether, or in a collodion mixture. The strength should be about ten per cent., and the application should be confined to the lesion proper.

Verruca plana may be favorably influenced by applications which produce desquamation. For this the following may be used with advantage, in full strength or slightly reduced with water: ℞ Calcis vivæ, 15.00; sulphur. sublimat., 30.00; aquæ, 300.00. M. Boil down to 180 c.c. and filter. Sig.: Vleminck's solution.

Verruca senilis yields readily to radiotherapy; comparatively few exposures are required, and the results are most excellent.

Prognosis.—Verrucæ are usually very amenable to treatment; in fact, many disappear spontaneously, which accounts for the multiplicity of vaunted remedies. Senile warts may develop into epitheliomata; these may be quickly removed by radiotherapy.

Ernest L. McEwer.

VERSION. See *Obstetric Operations.*

VERTIGO.—Definition.—A condition characterized by loss of the sense of bodily equilibrium. It is accompanied by subjective dizziness, by partial or complete loss of power to stand erect and to walk in a straight line, and in severe cases by nausea and vomiting.

The sense of equilibrium should be ranked among the special senses. It is but indirectly dependent upon sight, hearing, and touch, and it has, we now believe, a special nerve organ, which is used for this purpose and no other. Any interference with the function of this organ causes vertigo, just as any interference with the eye causes blindness, or with the ear, deafness; in any case the degree of impaired function varying with the intensity of its cause.

The sense organ of equilibrium consists of: (1) a cortical centre or area, apparently located in the cerebellum, and communicating by connecting fibres with various nuclei in the medulla and pons; (2) a nerve trunk, which forms the inner root of the eighth cranial nerve (auditory), passes with it into the internal auditory meatus, and is distributed, under the name of vestibular branch, to the vestibule; (3) a peripheral end organ, consisting of the semicircular canals, the utricle and saccule. These structures contain the peripheral terminations of the nerve, which, generally speaking, consist of hair cells. Briefly, these hair cells are supposed to be acted upon by currents in the endolymph, the currents being caused by changes in position of the head. The three semicircular canals correspond to the three dimensions of space. For further particulars see the article on *Audition*, in Vol. I. of this Handbook.

Symptomatic Vertigo.—In view of the extent and complicated anatomy of the organ, it is not surprising that its functions may be interfered with by many causes other than organic disease of its structure. Disease or injury of neighboring organs is of course particularly liable to cause such interference, and hence vertigo is a common symptom of ear disease. Equally, of course, is vertigo found in various diseases of the brain and spinal cord.

Anything which causes changes in the blood supply of the organ (anæmia, hyperæmia) may inhibit its normal action. Poisoning by certain drugs, or by bacterial toxins, or by auto-intoxications, such as constipation or gout, will do the same.

Of distant troubles causing vertigo, the most frequent are the various disturbances of digestion. In these cases the vertigo is usually slight and transient, and is relieved by measures which cure the indigestion. An acquaintance of the writer, a physician about forty years of age, has frequent attacks of vertigo whenever there is an accumulation of gas in his stomach or intestines. As his digestion is not strong, these attacks are troublesome. In his case the vertigo is severe, and he has even fallen to the floor under its influence. Getting rid of the gas, by mouth or rectum, gives him instant relief. It is probable that his trouble is due to disturbance of the circulation, consequent upon pressure of the distended bowel from below through the diaphragm, interfering with the heart's action. The prompt relief obtained by expulsion of the gas goes to disprove the presence of toxins.

Constipation vertigo, in its slighter forms, is common enough. It often occurs in conjunction with headache. The only effective treatment is the administration of a brisk cathartic.

Gouty vertigo is allied to constipation vertigo, and the distinction between the two conditions is not always clear. Vertigo is seldom seen in typical cases of acute gout. It comes more often in the irregular forms, with migraine, catarrh of the respiratory and digestive mucous membranes, and pain and stiffness in various joints and muscles. It is often severe, and may be the only symptom which calls the patient's attention to his condition. It is caused by uric acid and other waste products of half-burned albumin, which accumulate in the system and act as poisons, probably directly through the tissues. The diagnosis rests upon the presence of other symptoms of gout, upon the condition of the urine, and upon the absence of signs of disease of the internal ear.

Various disturbances of the circulatory system may cause vertigo. The trouble may lie in the blood, the heart, or the vessels. Of the blood diseases, pernicious anæmia is probably the one most frequently attended by vertigo, but it is also seen occasionally in chlorosis. It is probably caused by cerebral anæmia. It is not usually severe or important. The diagnosis depends upon other signs of anæmia, and the treatment is the treatment of the general disease. Certain cases of leukæmia and Hodgkin's disease exhibit vertigo as a symptom. It may be very severe, in which case it is accompanied by signs of severe general cerebral disturbance, and is due to leukæmic lymphadenomata in the skull (Friedreich).

Cardiac vertigo is seen in many forms of heart disease. It is a common and early symptom of fatty degeneration of the heart. It usually comes on in attacks, which vary in severity over a wide range. The vertigo may be very slight, attended with nausea or slight faintness, or it may be more severe, attended with actual syncope, followed by a period of unconsciousness, and resulting in paralysis, loss of memory or intellectual power, or even death. This form of vertigo is caused by cerebral anæmia, and the diagnosis rests upon the presence of other signs of fatty heart, plus the absence of signs of ear trouble. The exact diagnosis of fatty heart is always difficult and may be impossible, but the undoubted evidence of cardiac incompetency, the absence of signs of valvular trouble, and the typical nature of the vertiginous attack, will usually give a clew.

Vertigo also occurs in other forms of heart disease, especially in disease of the aortic valves, either stenosis or insufficiency. Here the giddiness is slight and more or less constant, being much the same in either condition of the valves. The cause is disturbed brain circulation, and the diagnosis is made by examining the heart.

In aortitis and disease of the coronary arteries vertigo is often noted, especially in connection with attacks of angina. There is nothing characteristic about this form, and it is usually overshadowed by the pain, dyspnœa, sense of impending death, etc., which belong to the attack. In general arteriosclerosis vertigo is sometimes seen, due probably to changes in the cerebral vessels. This variety belongs among the encephalic vertigos.

In certain general systemic infections vertigo is often seen. Notable among these are influenza, typhus and typhoid fever, malaria, and plague. Vertigo in influenza is seen often; it may be severe, but usually does not last many days. Licéaga ("Twentieth Century Practice of Medicine," vol. xv., p. 286) declares that it is "constant and precocious, and appears whenever the patient attempts to sit, to stand, or even to raise his head." In typhoid fever vertigo is seen during the incubation period and at the beginning of convalescence. It occurs probably in about ten per cent. of the cases. At the outset of an attack of *bubonic plague* vertigo is said to be common. All these forms are caused by the toxin of the disease acting upon the brain or its circulation. They are not accompanied by deafness. They are in many cases merely a symptom of exhaustion, and they do not remain permanently after recovery from the disease.

The vertigo which follows the more severe forms of malarial fever, however, is different. It comes on after the disease has lasted for some time, is attended with deafness and tinnitus, and seems due to inflammation in the internal ear. It is rare. It belongs to the pernicious tropical forms, and there is ground for doubting if it be not due to the quinine rather than to the malaria. Ferreri reports two cases.

Certain drugs in toxic doses cause vertigo. Prominent among these are alcohol, aniline and its derivatives, quinine and salicylic acid. Alcohol probably acts by paralyzing the cortical areas in the cerebellum. Aniline acts in the same way. Quinine and salicylic acid, on the other hand, probably act directly upon the internal ear, since poisoning by either of them causes deafness and tinnitus as well as vertigo. Such cases rarely present difficulties of diagnosis.

Vertigo is also seen in certain diseases and disturbances of the central nervous system, both functional and organic. Seasickness comes under this head, being apparently caused by overexertion of the sense organ of equilibrium. The motion of the ship sends the endolymph flowing rapidly through the semicircular canals, agitating the hair cells violently, and thus interfering with their function. All symptoms of seasickness, it is well known, may be produced by rapid rotation of the body, and the fact that measures directed to the nervous system are the only ones that have been found effective in combating this malady, lends support to this view.

Neurasthenic vertigo is not uncommon. The attacks are short and not very severe, but often occasion much alarm. The diagnosis rests upon other symptoms present, and treatment is directed to the neurasthenia.

Epileptic vertigo is seen oftenest in attacks of *petit mal*. It is paroxysmal and brief. The patient feels dizzy, and perhaps falls to the ground, but recovers at once, and the vertigo disappears as the fit passes (Church).

Of the organic degenerative lesions of the general nervous system, vertigo is found often in tabes dorsalis. This vertigo is not to be confounded with the regular and constant ataxia. The two are quite distinct, and ordinarily, however extreme the ataxia, the patient does not suffer from subjective vertigo. When this occurs it is paroxysmal, and may be accompanied by vomiting and great prostration. In multiple spinal sclerosis (Church) vertigo often occurs. Here it is sometimes due to destruction of the central organ or the nerve trunk, and may present the type of Ménière's disease. These vertigos are to be diagnosticated and treated in connection with the underlying disease which causes them.

Of encephalic diseases any lesion interfering with any part of the sense organ of equilibrium may cause vertigo. It is most common in tumors or abscesses of the cerebellum and pons, in hemorrhage, or more rarely in basilar meningitis. It is constant and severe, often accompanied by nausea and vomiting, but except in connection with

other symptoms it is not reliable for diagnostic purposes (Starr).

Vertigo also occurs in many cerebral diseases, such as endarteritis, general paresis, cerebral hemorrhage, cerebral syphilis. If the lesion be cerebral the vertigo is usually slight and transient.

Certain diseases of the eyes cause vertigo, especially ocular palsies. This is sometimes reflex and sometimes, probably, suggestive, the result of the double image. These cases can be relieved by blindfolding one eye, or by rectifying the muscular anomaly when possible.

Suggestive vertigo is seen often in persons who for the first time look down from a great height. It is purely psychic, and not a true vertigo at all.

Aural Vertigo.—This may occur as the result of any diseased condition affecting any part of the ear, from the auricle to the encephalic opening of the internal auditory meatus. It is specially common in labyrinthine disease. There is a type of otitis interna which gives rise to a definite and characteristic variety of vertigo, known as Ménière's disease. Anatomically it consists usually of a hemorrhage into the labyrinth, which may be caused by violence, such as a blow upon the head, or certain operative precedures upon the tympanum, such as mobilization of the stapes (Dench). Politzer says with reason that it is not the hemorrhage, as such, that causes the symptoms, but the effect of the extravasated blood upon certain structures of the membranous labyrinth. Therefore it is possible that there should be a considerable extravasate in the labyrinth without causing vertigo, or, on the other hand, a very small amount might produce it, according to whether or not the ampullar nerves are interfered with.

The true, typical, apoplectic form of this trouble is rare. According to Politzer, Frankl-Hochwart has been able to collect only twenty-seven cases in all the literature. It begins with giddiness, of such degree that the patient falls to the ground. He also suffers from intense nausea, vomiting, marked deafness, and sometimes a subjective noise in the ear like a loud report (Starr), or loud and distressing tinnitus (Politzer). The loss of hearing is usually bilateral. It may or may not be complete, but it is always severe. The course of the disease is to a slow and incomplete recovery. The nausea and vomiting first subside, and then, in the course of ten days or two weeks, the giddiness improves and the patient slowly regains his equilibrium. The deafness, however, persists in very nearly its first intensity, and the gait is apt to be more or less unsteady for months or years. Treatment must be on general principles—cold and local depletion at the outset, with rest in bed, catharsis, and nerve sedatives as required, morphine if necessary. After convalescence is established, a general supporting and building-up treatment is indicated. Politzer recommends potassium iodide, gr. xv. a day for three or four weeks, and also pilocarpine, gr. $\frac{1}{10}$–$\frac{1}{5}$ a day.

The diagnosis of true labyrinthine vertigo rests upon: 1, Its intensity—it is always severe; 2, the accompanying deafness and tinnitus; and 3, the absence of signs of (*a*) cerebral disease, or (*b*) middle-ear trouble. In Ménière's disease the symptoms are usually bilateral; in traumatic cases they may be unilateral. A very interesting case of this sort is reported by Starr. A fireman fractured the base of his skull and tore the left auditory nerve. His chief symptoms were complete deafness on the left side and constant and agonizing sense of rotation of his body on its longitudinal axis, so that if left alone in bed he would roll over and over in the opposite direction to overcome this feeling. He died on the fifth day after his accident.

Other forms of aural vertigo are less severe and less typical. The vertigo that occurs as the result of trouble in the external auditory canal (cerumen, furuncle) is slight and transient. Occasionally chronic aural catarrh will cause a certain degree of vertigo, which may be quite severe. And in chronic suppurative otitis, with cholesteatoma, vertigo may occur at any time as the result of erosion of the external semicircular canal. The writer has seen two such cases, one of which was operated upon by Dr. Whiting, of this city, with complete relief. Vertigo occurring in these cases, at the end of a long period of suppuration, is a dangerous complication, and calls for prompt surgical interference.

It is the firm conviction of the writer that in every case of vertigo, whatever be the history and circumstances, the condition of the ears should be carefully and thoroughly investigated. *Donald M. Barstow.*

VESICO-VAGINAL FISTULA. See *Vagina, Diseases of.*

VETERINARY SCIENCE IN ITS RELATION TO PUBLIC HEALTH.—Veterinary science includes in its domain a complete knowledge of the domesticated animals. It is not limited, as many suppose, to their anatomy, physiology, pathology, and therapeutics, but, in addition to these subjects, it covers zootechnics, or the economical production of animals, veterinary hygiene, or the maintenance of animals under healthful conditions, veterinary sanitary science, or the control of contagious diseases, the exclusion of exotic contagion and the inspection of animal food products. It may be said, therefore, that it is the province of veterinary science, (1) to aid in producing a supply of animal food of the best quality and in the greatest abundance; (2) to protect the sources of this food supply so far as possible from the ravages of communicable diseases; (3) to prevent the use of animal food products contaminated by disease; (4) to guard mankind from the plagues and parasites of animals which may be transmitted to the human subject; (5) to make scientific investigations of animal diseases which will advance our knowledge of these diseases and of general pathology. All of these lines of work operate directly to improve the public health.

The Animal Food Supply.—An abundant supply of wholesome food is necessary for the preservation of the public health; and as the food supply deteriorates in quality or diminishes in quantity the conditions of life become more difficult. Want, distress, and misery result. Following the impoverishment of the body come disease and an augmented mortality. Famine and pestilence are words which the long and bitter experience of the human race has associated together. The scarcity and bad quality of food is felt first and most severely where the population is most dense, and where a large part of the people, at best, have a serious struggle for existence. It follows, of course, that as a country develops and becomes more densely populated, as cities multiply and contain a greater number of people who even in times of abundance must eat inferior food, the effect of deteriorations of the food supply becomes more evident. A nation with an abundant supply of good food is already well on the way to prosperity and healthfulness.

Animal food forms a most important part of the general food supply. The stock of animals maintained in the United States at this time for the production of human food is approximately 17,105,227 milch cows, 44,659,206 other cattle, 63,964,876 sheep, 46,922,624 swine, and 250,681,593 fowls of various kinds. The raising, marketing, and slaughtering of these animals, and the production of the milk, butter, and cheese involve many problems which the veterinarian can solve, or at least should help to solve. And just as the increasing density of the human population brings new problems to the health officer and sanitarian, so an increase in the number of animals and the change from natural to artificial conditions bring new problems to the veterinarian. When animals are allowed to roam over large tracts of land, seldom or never stabled, and not pressed for the largest attainable product, when traffic between different sections of the country is at a minimum, the animals are found in the most vigorous and healthful condition. On the other hand, when animals are crowded together, stabled, fed to their highest capacity, and become a subject of traffic, disease and parasites multiply; questions of ventilation, of general sanitary methods, of proper feeding, of pro-

tection from contagion and parasites arise and become more and more urgent.

The quantity of animal food consumed in the United States cannot be very accurately estimated. Under the federal meat inspection service there were slaughtered in the year ending June 30th, 1902, 6,115,805 bovine animals, 7,434,478 sheep, and 25,277,107 hogs. In addition, many of the same kinds of animals were slaughtered for local consumption or in establishments where no inspection has been instituted. There is no systematic inspection of poultry at the time of slaughter, but the production of an abundant supply of poultry and eggs must depend somewhat upon the preservation of fowls from contagious diseases, and the knowledge through which this is to be accomplished must come from veterinary sanitary science.

The quantity of milk in its natural condition consumed in the United States is about 21,751,258,560 pounds, of condensed milk 172,647,355 pounds, of butter 1,465,299,727 pounds, of cheese 278,538,146 pounds.

These figures show the enormous extent to which animal products enter into the food supply of the country, and they indicate the importance of establishing safeguards which will make it reasonably certain that such products are wholesome and will not prove a source of disease to the consumers. Dairy cows should be inspected from time to time to determine that they are free from disease, and especially that they are free from diseases communicable to man. Dark, unventilated, damp, and filthy stables should be abolished, and it should be insisted that animals be kept under hygienic conditions. Milk is too often sold from cows suffering from tuberculosis, actinomycosis, metritis, mastitis, and other diseases which may seriously affect its quality.

It is equally important that animals should be inspected at the time of slaughter. A certain proportion of diseased animals will be found even among those which superficially appear the most healthy. It is a common practice to ship to market animals which no longer thrive on the farm; and while in many cases the owner does not know what ails them, it often happens, as with hogs affected with cholera, that they are shipped to market because they are known to be infected, and that the losses among them will be heavy if they are retained upon the farm. In addition to the animals diseased when they leave the farm, there are many which become bruised, wounded, crushed, and otherwise badly injured in transit. Some of these when they reach the abattoirs are suffering from abscesses, septic infection, abortion, and various other pathological conditions the result of injuries. These conditions can, of course, be recognized and graded as to their seriousness only by the trained veterinarian.

The Protection of Animals from Infectious Diseases.—Probably the most important line of work for preserving the food supply both in quantity and quality is that which controls, eradicates, and excludes the contagious and infectious diseases of animals. This is particularly necessary at the present time, when transportation routes and means of communication between all parts of the world have multiplied, when facilities for shipping animals and animal products have been greatly increased, and the time required to bring these from the most distant part of the world has been enormously diminished. We have reached a degree of development in these matters when it may be said that the time of transit is no longer a protection against the importation of contagion from the most distant countries.

As the veterinarian examines the condition of animals in other countries he finds that Asia, the Philippines, and Africa are overrun with rinderpest, that most deadly of all cattle diseases. He finds the contagious pleuropneumonia of cattle in Asia, Australia, Africa, and in several countries in Europe. He finds epizootic aphtha, or foot-and-mouth disease in Europe, Asia, and South America. He finds surra in India and in the Philippines. He finds Texas fever in most warm countries of the world, including South Africa, Australia, South and Central America, the West Indies, Mexico, and the southern parts of the United States. He finds sheeppox, scabies, anthrax, hog cholera, and various other destructive diseases widely disseminated throughout the world. The country must look to him to exclude such diseases, which would not only diminish the food supply, but which would increase the proportion of diseased animals coming to the abattoirs.

The United States, fortunately, has been free from some of the worst of these plagues, but distance is no longer the barrier that it has been in the past, and active measures are now required against them. Europe has again and again suffered the most terrible losses from invasions of this character. And at this writing, foot-and-mouth disease has been prevalent in most of the countries of continental Europe for more than fifteen years. Considering the large number of live animals of various kinds which annually enter the United States from abroad, including domesticated animals, menagerie animals, and those for zoological parks, pets, etc., also, the enormous quantities of wool, hides, and hair imported, it is plain that there are many channels through which contagion may be carried.

Within the last year there has occurred, in the New England States, an outbreak of foot-and-mouth disease which started near the docks of Boston, undoubtedly from imported contagion, and which has been stamped out only by the most prompt and rigid measures. With this disease in South America threatening us from the south; with rinderpest in our Philippine possessions; with foot-and-mouth disease and pleuropneumonia still existing in Europe, it is plain that nothing less than constant vigilance can preserve our flocks and herds from these plagues.

The measures adopted in the United States for excluding exotic contagion consist of an inspection of all susceptible animals, the quarantine of ruminants and swine which come from infected countries, and the disinfection of the hides of neat cattle. The period of quarantine varies from fifteen to ninety days, the animals being held in the regularly established quarantine stations of the Government. Cattle imported for breeding purposes must be tested with tuberculin to guard against tuberculosis. An inspector from the United States is now stationed in Great Britain to make such tests before the animals are purchased, as it has been found that a very large percentage of some of the principal British breeds are tuberculous. On the other hand, animals from the Channel Islands have been found free from tuberculosis and are no longer tested.

The measures for controlling contagion within the United States consist of an inspection at the principal stockyards, and at other convenient points for supervising the interstate traffic. This inspection is maintained by the Federal Government and has for its object at present the control of Texas fever of cattle, scabies of sheep and cattle, and hog cholera. In addition, many of the individual States and municipalities maintain a service for the repression of glanders, tuberculosis, rabies, Texas fever, scabies, and other diseases of the domesticated animals.

The Protection of Mankind from the Communicable Diseases and Parasites of Animals.—That there are certain diseases of animals which are communicable to man has long been known. There are also parasites of animals which likewise may be communicated and which produce results more or less serious according to the species of parasite which is involved. Among the most common of these diseases and parasites are : (1) Glanders, a disease of the genus *Equus*, generally fatal when contracted by man; (2) anthrax, a disease of horses, cattle, sheep, and swine, appearing in man either as malignant pustule or as internal anthrax, and often fatal; (3) tuberculosis, a disease common in cattle and swine, but also occurring in horses, sheep, goats, dogs, poultry, cage birds, and menagerie animals; (4) rabies, a disease of the genus *Canis*, communicable to all warm-blooded animals and to man; (5) epizootic aphtha, commonly known as foot-and-mouth disease, a very infectious malady of cattle,

sometimes communicated to the consumers of the milk of diseased cattle; (6) *Cysticercus bovis*, found in cattle, is the larval form of the tapeworm of man known as *Tænia saginata*; (7) *Cysticercus cellulosæ*, found in swine, is the larval form of the tapeworm of man known as *Tænia solium*; (8) the *Trichina spiralis*, a common parasite of swine, may develop in man and sometimes produces fatal results; (9) the *Echinococcus* found in the lungs, liver, and other organs of the meat-producing animals is the cystic phase of the *Tænia echinococcus* of the dog.

It is evident that the most satisfactory way of protecting man from this source of danger is to eradicate these diseases and parasites so far as possible from the domesticated animals. Hence all veterinary sanitary work having this object in view has a direct bearing upon the public health. As complete eradication cannot be accomplished for many years and in some cases not at all, there must be constant efforts for repression and control. People must be made familiar with the dangers; too close association with animals should be avoided; the inspection of meat and of dairy cows should be universal; swine flesh should be well cooked; hides, wool, and hair, often infected with the anthrax bacillus, should be handled with suitable precautions; biological products used for the prevention or cure of human diseases should be surrounded with every safeguard to avoid contamination.

Investigation of Animal Disease as to its Influence on Human Pathology.—The investigation of the diseases of animals, and experiments conducted upon animals, have done much to advance the knowledge of pathology and therapeutics. The use of cowpox virus to vaccinate against smallpox has been of inestimable value for the control of this scourge of the human race. The existence of glanders and rabies in man has been proved by the successful inoculation of susceptible animals from suspected cases of these diseases in the human subject. The study of silkworm disease and anthrax in animals established the germ theory of contagion.

Investigations of the fowl-cholera microbe first proved that a virulent virus might be artificially attenuated to such a degree that it might be used as a vaccine to prevent disease. Experiments with the toxin developed by the bacillus of hog cholera showed that immunity might be developed by the use of such toxins. This conclusion revolutionized the prevailing ideas of immunity, and led to the researches which gave us the knowledge now possessed relative to toxins, antitoxins, and the nature of immunity. The study of Texas fever in cattle showed that the protozoan organism causing the disease was dependent upon the cattle tick (*Boophilus annulatus*) for one stage of its existence and for its conveyance from animal to animal. Later investigations brought out the fact that certain diseases of man, such as malaria and yellow fever, likewise required two distinct organisms for their production. The study of tuberculosis in animals directed attention to the communicability of the disease, and comparative inoculations of animals have demonstrated that the bacilli from certain human cases were identical with bovine bacilli. Doubts as to the transmission of tuberculosis from animals to man have thus been removed.

These instances are referred to as illustrations of the close relation between human and veterinary pathology, and of the influence of the latter upon the development of the former. It has been well said that human and veterinary medicine are not merely sister professions, but they are sister branches of the one great profession of medicine. The closer the relations existing between these two branches of the medical profession, and the more each utilizes the knowledge of the other that may be applicable to its work, the more successful will be our efforts for the amelioration of suffering, the prolongation of life, and the uplifting of humanity.

The limits of this article are such that it is not advisable to attempt a complete description of the several diseases of animals liable to be communicated to man or injuriously to affect his food supply. There are, however, important questions connected with these diseases which should receive consideration, and if the author in confining himself to such subjects as he deems essential, has produced an article that appears incomplete, it should be remembered that many topics which might have been introduced here are discussed elsewhere in this HANDBOOK by other writers.

TUBERCULOSIS OF ANIMALS.

General Characters.—The disease caused by the *Bacillus tuberculosis* affects a wide range of animal life, and is especially seen outside of the human subject, in the various species of the monkey tribe, in most kinds of menagerie animals, including mammals, birds, and reptiles; in all the domesticated animals, but more particularly in cattle, swine, and poultry; in cage birds; and in frogs and fishes. Taken from such widely different sources the bacilli are found to differ considerably both morphologically and biologically. For example, the temperature limits within which the mammalian bacillus may grow are approximately 86° to 105.8° F.; the avian bacillus, however, may multiply in temperatures all the way from 77° to 113° F.; while the reptilian and piscine bacilli have been observed to multiply in those from 50° to 98.6° F. Notwithstanding these biological differences the mammalian bacillus has been so modified that it has acquired the piscine and reptilian characteristics; and the avian has been made to take on the mammalian characteristics. The modifications which have been noticed by various investigators relative to the length, breadth, smooth or beaded form, and appearance of the colonies on various media, are not entirely constant in the bacilli obtained from the same species of animals and change very materially on different culture media. While these characters may aid in determining the source of a given bacillus they are not absolutely certain in their indications.

The avian type of tuberculosis is not readily communicated to any mammalian species and probably is very slightly if at all dangerous to man. Parrots and small birds, however, contract mammalian tuberculosis, and this is sometimes very virulent for mammals, and is believed to be dangerous for the persons who are closely associated with them. There is considerable difference between the bacilli that are generally obtained from the human subject and those derived from bovine animals. This relates both to the morphology and to the virulence. We, therefore, often speak of the human and bovine types of bacilli. Swine are most frequently found affected with the bovine type. The constancy of these types is doubtful, but in certain instances a given strain of bacilli has been known to retain its characteristics for a long time (one or more years) after being transferred to a different species of animals.

Bovine animals are the ones most frequently found tuberculous, and they are probably in most cases the source of the disease in the other domesticated species. Bovine tuberculosis has therefore attracted more attention than that of other animals and is most interesting to the sanitarian. Many points relative to this disease have been in doubt, but the investigations of recent years have added much to our knowledge of it, and we are now in a position to speak positively in regard to the principal questions at issue.

Distribution and Prevalence.—Bovine tuberculosis is a disease widely distributed and of great frequency in certain countries. Slaughter-house statistics of Prussia show 16.6 per cent. of the cattle and 2.41 per cent. of the swine to be tuberculous; in Saxony the percentage is 29.13 with cattle and 3.10 with swine; in the city of Leipsic there were found 36.4 per cent. with cattle and 2.17 per cent. with swine. Of 20,850 bovine animals in Belgium tested with tuberculin in 1896 48.88 per cent. reacted. Of 25,439 tested in Denmark from 1893 to 1895 49.3 per cent. reacted, and of 67,263 tested from 1896 to 1898 32.8 per cent. reacted.

The condition of Great Britain in this respect is particularly interesting because most of the animals imported for improving the stock of the United States are of British origin. The returns from testing British cattle with tuberculin, supplied by the Royal Veterinary College, as stated in March, 1900, showed that among 15,392 animals tested, 4,105, or 26 per cent., reacted. Of 300 head killed near Edinburgh for pleuropneumonia, 120, or 40 per cent., were tuberculous. Of 4,160 killed in England for the same reason, 20 per cent. were tuberculous. Of 398 bovine animals taken haphazard in the city of Manchester, 120, or 30 per cent., were tuberculous. The testing of the Queen's herd at Windsor showed that 36 out of 40, or 90 per cent., were tuberculous. The British Dairy Farmers' Association made investigations in 1899 with a view to some more definite understanding as to the possible extent to which tuberculosis exists in dairy cattle. Nine herds were selected for testing, and these contained 461 cows and 12 bulls. Of these animals 188, or 40.8 per cent., reacted.

During the years 1901 and 1902 a veterinary inspector has been stationed in Great Britain by the Bureau of Animal Industry, whose duty it is to test animals which are to be exported to the United States. In 1901 there were tested 720 animals, of which 74, or 10.28 per cent., reacted. In 1902 the animals tested reached the number of 935, of which 156, or 16.68 per cent., reacted. Curiously enough but one reaction was obtained, and that of a doubtful character, among 377 cattle from the islands of Jersey and Guernsey, but 99 cattle of the Jersey and Guernsey breeds which had been in the herds of Great Britain gave 34.3 per cent. of reactions. Some breeds appear to be much more seriously infected than others. Thus, of 42 British Jerseys 54.76 per cent. reacted; of 362 Aberdeen-Angus 28.73 per cent. reacted; of 33 Ayrshires 24.24 per cent. reacted; of 228 Shorthorns 23.25 per cent. reacted; of 36 Galloways 16.67 per cent. reacted; while of 428 Herefords but 3.97 per cent. reacted.

It is especially unfortunate that tuberculosis has developed to this extent in the principal British breeds and is allowed to continue its propagation. These breeds are the best in the world, and are sought for to improve the native cattle of various parts of the world. They are particularly in demand in the United States, and as might be expected they have carried tuberculosis wherever they have gone. From Australia, Argentina, and Canada we have similar accounts of the importation of British cattle and the spread of bovine tuberculosis. The United States Government has endeavored to exclude tuberculous cattle by requiring a tuberculin test. For British cattle this is made by a United States inspector located in Great Britain, and for Canadian cattle it is made by the officials of the Dominion Government.

State.	Number tested.	Number tuberculous.	Per cent. tuberculous.
Vermont	60,000	2,390	3.9
Massachusetts	24,685	12,443	50.0
Massachusetts, entire herds	4,093	1,080	26.4
Connecticut	6,300	...	14.2
New York, 1894	947	66	6.9
New York, 1897–98	1,200	163	18.4
Pennsylvania	34,000	4,800	14.1
New Jersey	2,500	....	21.4
Illinois, 1897–98	929	....	12.0
Illinois, 1899	3,655	560	15.32
Michigan	....	....	13.0
Minnesota	3,430	....	11.1
Iowa	873	122	13.8
Wisconsin: Experiment station tests—			
Suspected herds	323	115	35.6
Non-suspected herds	935	84	9.0
State veterinarian's tests—			
suspected herds	588	191	32.5
Tests of local veterinarians under State veterinarian on cattle intended for shipment to States requiring tuberculin certificate	3,421	76	2.2

The percentage of the cattle in the United States affected with tuberculosis has not been accurately determined, and most of the herd tests have been made where there was reason to suspect the existence of the disease. The statistics of such tests show a higher percentage of reacting animals than would the average of all the cattle in the respective States. From a recent review by Drs. Russell and Hastings, of the Wisconsin Agricultural Experiment Station, of the tests of cattle which have been made in the United States, the preceding summary is presented.

The beef cattle coming to our markets are still quite free from tuberculosis. Of 5,559,969 cattle slaughtered during the year 1902, but 8,096, or 0.14 per cent., were sufficiently affected to cause the condemnation of carcasses or of parts of carcasses. Of 25,277,107 swine inspected at slaughter in the same year, 19,627, or 0.077 per cent., were so affected as to cause condemnation of either a part or the whole carcass. This is approximately one-half the proportion found in beef cattle. The inspection statistics show that the percentage of condemnations with both cattle and swine is increasing from year to year.

With hogs tuberculosis is a disease generally contracted from the ingestion of infected food, and hence, as the disease is allowed to spread among cattle, it will become more frequent with the hogs that follow the cattle in the pastures or that eat the skim milk, buttermilk, and other waste products of the dairies. The disease is more acute with swine and has a greater tendency to generalization than with cattle, and consequently there is more danger of the meat containing the bacilli.

Tuberculosis is not pre-eminently a disease of poor, neglected, underfed scrub cattle, as some have supposed, but on the contrary its ravages have been seen more particularly among the better class of cattle. This is accounted for by its introduction and spread through imported, pure-bred stock which entered and infected many of the best herds in the country. From these herds of improved stock it has extended to the dairy herds and common cattle.

A brief list of infected herds which have been carefully studied is inserted to show the extent to which the disease develops and the difficulty of building up a herd of good cattle under the best conditions and keeping it free from this disease:

Herd of	Number in herd.	Number tuberculous.	Per cent. tuberculous.
Soldiers' Home, Washington, D. C.	63	53	84
Massachusetts Agricultural College	32	25	78
New Jersey Agricultural Experiment Station	42	25	60
Vermont Agricultural Experiment Station	33	21	64
Ohio Agricultural Experiment Station	30	14	46
Texas Agricultural Experiment Station	21	10	48
Wisconsin Agricultural Experiment Station.	30	26	86
Kansas Agricultural College	56	15	27
Government Hospital for the Insane, Washington, D. C.	102	79	77
Maine Agricultural Experiment Station *	..	..	..

* So badly diseased that entire herd was slaughtered in 1886.

Diagnosis of Tuberculosis in Animals.—*The Tuberculin Test.*—The diagnosis of tuberculosis in animals by an ordinary clinical examination during life is in most cases difficult and often impossible. When cough, marasmus, enlarged glands, and râles are found in cows it is not difficult to reach a conclusion, but such cases are exceptional. Many cows, which show no symptoms of disease during life, are found on post-mortem examination to be seriously affected. This is even more likely to be true of breeding animals of the beef types. In hogs this disease is rarely recognized during the life of the animal.

The discovery of tuberculin and of its power to produce a rise of temperature in tuberculous individuals has

been of the greatest value to the veterinarian in diagnosing the tuberculosis of animals, indeed, it may be said that the use of this agent is essential to the control and eradication of this plague. There is a consensus of opinion that every animal which reacts is tuberculous; but it must be understood that every rise of temperature is not necessarily a reaction. There may be other causes acting to increase the temperature during the same period that an increase would be expected from the tuberculin. It requires some skill to decide correctly as to what constitutes a reaction. The principal points considered are: (1) the initial temperature should not be abnormally high —not over 102.5° F.; (2) to constitute a reaction the rise should be not less than 2° F.; (3) the temperature should go above 104° F.; (4) the rise and fall of the temperature should be gradual so that when charted it shows the tuberculin curve.

Some animals which have tuberculosis do not react to tuberculin. These are generally in such an advanced stage of the disease that a diagnosis by other means may be made, or they are cases in which the disease has been arrested and the lesions are calcified or encysted. A tuberculous animal, which has already received one or more doses of tuberculin, may fail to react for this reason, particularly if the drug has been administered within two or three months. Some cattle owners use tuberculin in this manner to prevent cows reacting on an official test, and it is alleged that breeders in Great Britain have administered antipyretics to accomplish the same purpose.

Tuberculin may be used for diagnosing tuberculosis in all species of animals, and is especially valuable for the selection of experimental animals which are free from this disease.

In making the tuberculin test the temperature of the animal to be tested is first taken at intervals of two or three hours for a sufficient length of time to establish the normal temperature of the individual under the ordinary conditions of life. The proper dose of tuberculin is then injected under the skin with a hypodermic syringe. This injection is usually made late in the evening and the temperature is taken every two hours the following day, beginning early in the morning and continuing until late in the evening if a complete record is desired. From a study of a large number of such records it appears that in general the rise of temperature begins from five and one-half to six hours after the tuberculin is injected, reaches its greatest height from the sixteenth to the twentieth hour, and then gradually declines, becoming normal again by the twenty-eighth hour.

It has been charged that tuberculin is injurious to the animals upon which it is used, causing shrinkage of the milk, abortion, and aggravation of this disease. The evidence brought forward is not sufficient to sustain these assertions. Those who have had most experience in testing cattle are of the opinion that tuberculin is harmless in the dose used for this purpose. Abortion is common with dairy cows and would occur sometimes after the tuberculin tests as a mere coincidence. The milk secretion of cows may also be reduced by the excitement incident to taking the temperature, particularly if this is done by persons who are strange to them. It is possible that in some cases tuberculosis is aggravated by the tuberculin test, but in general no effect of this nature is observed with cattle. It may be concluded, therefore, that tuberculin, as used for testing cattle, has no appreciable effect upon the general health of the animals, and that it may be used without hesitation whenever it is desirable to know whether any animals in a herd are affected with tuberculosis.

Hereditary or Congenital Tuberculosis.—Tuberculosis is generally contracted by contagion from animal to animal, but a small proportion of calves are affected before birth. There are few statistics which indicate accurately the proportion of cases in which the disease is thus transmitted. Siedamgrotzky has compiled statistics from the slaughter-house returns in Saxony, from which the following data are taken:

Slaughter-House Statistics of Saxony.

Year.	Per Cent. Tuberculous	
	Calves.	Adult cattle.
1895	0.24	27.48
1896	.21	26.72
1897	.26	29.13

This table indicates that in a country where about twenty-seven per cent. of the adult cattle are found to be tuberculous, approximately 0.25 per cent. of the calves are tuberculous. If we admit that fifty per cent. of the cows have the disease, we should arrive at the conclusion that one-half of one per cent. of the calves from tuberculous mothers are affected at the age of slaughter. It would be difficult to say what proportion of these contracted the disease from the mother's milk after birth, but probably the greater part of such cases are congenital. The small proportion of calves from tuberculous mothers which suffer from hereditary tuberculosis has made it desirable in certain cases to allow breeding from valuable cows which have the disease. If the calves are taken from the mothers after feeding once or twice upon the mother's milk and are afterward fed with milk of sound cows, experience shows that not over one or two per cent. at most are afterward found to have the disease.

Tuberculosis of the Udder.—Only a small proportion of the cows which react to tuberculin have lesions of tuberculosis in the mammary glands. Siedamgrotzky's summary of the slaughter-house statistics of Saxony from 1888 to 1897 covers 70,156 tuberculous cows, of which 1,040, or 1.4 per cent., had tuberculosis of the udder. The same authority states that Röckl found 1.62 per cent. of udder lesions among tuberculous cows in Germany. It would seem, therefore, that we might assume that in round numbers 1.5 per cent. of cows reacting to tuberculin may be expected to have lesions in the mammary glands. This subject is of considerable importance, because it has been assumed by some writers that the milk of tuberculous cows was dangerous only when the udder was directly involved; and evidently the milk must be more dangerous when there are such local lesions than when the tubercles are confined to other parts of the body.

Proportion of Reacting Cows in which the Milk is Virulent.—It has often been held that the milk of tuberculous cows is free from infective qualities until the mammary glands become affected. Numerous experiments have been made with the milk from reacting cows, some of which have given negative results, but in others it has been shown that from ten to sixty-six per cent. of the reacting cows gave virulent milk even when no lesions of the udder could be detected. In a recent investigation made by the pathological division of the Bureau of Animal Industry with fifty-six reacting cows it was found that twelve of these, or 21.4 per cent., at one time or another during the experiment gave milk which contained virulent tubercle bacilli. Taking all the researches on this subject, it is clear that the proportion of reacting cows giving infective milk is very much larger than the percentage of udder tuberculosis in tuberculous animals. The bacilli must, therefore, find their way to the mammary glands from the other organs of the body where the lesions are developing, and, passing through the capillary walls, gain access to the milk ducts.

Transmission of Bovine Tuberculosis to Man.—There has been much discussion over the question of the transmission of animal tuberculosis to man. Previous to the discovery of the tubercle bacillus there was much doubt as to whether the tuberculosis of cattle and human tuberculosis were identical. But when it was shown that each was produced by the *Bacillus tuberculosis*, there was a general disposition to accept the identity of the disease in the two cases and admit that it was communicable in either direction. Experimenters found, however, that

the tubercle bacilli, as observed in different species of animals, varied considerably in their biological characters, and that it was difficult to transfer them, by inoculation, from some species of animals to others. It was shown that inoculations of cattle with the sputum of tuberculous persons generally failed to produce serious results, while similar inoculations with tuberculous material from bovine animals were generally fatal. There was a disposition on the part of some authorities to conclude that there might be a difference between the tuberculosis of man and that of cattle, and that it was doubtful if the disease could be transferred either from the human subject to cattle or from cattle to man. These suppositions culminated in the address of Koch at the British Congress on Tuberculosis held in London in 1901.

In this memorable address Koch held, from the results of his experiments, that human tuberculosis could not be communicated to cattle, and that if bovine tuberculosis was communicated to man this was only to an insignificant extent, the cases occurring from this source not being greater, in his opinion, than those from hereditary tuberculosis.

Numerous experiments have since been made to determine this point, and it has been found that tubercle bacilli from human subjects vary greatly in their virulence and power to cause disease in cattle. A number of investigators have succeeded in isolating bacilli from human material which were as virulent for cattle as were the bacilli obtained from the bovine subject.

A German commission was appointed to investigate this question, and the results of its experiments have recently been made known by Kossel. This commission has been more successful in producing tuberculosis in cattle with bacilli from human sources than was Koch in his experiments upon which his London paper was based. Altogether, cultures from 39 cases of tuberculosis in man were tested according to the principles laid down by Koch. He concluded that human tuberculosis was not communicable to cattle, and that therefore if cattle were inoculated subcutaneously with cultures of bacilli from human subjects and a progressive and fatal disease was produced, this would demonstrate that the person had been infected with bovine bacilli. Of the 39 cultures tested, 19, or a little less than 50 per cent., did not produce the slightest symptoms in cattle. Nine cattle exhibited, in the prescapular glands, after the lapse of four months, foci which were mostly encysted, and which in any case showed no inclination to develop. In 7 of the cases more marked disease of the prescapular glands occurred, but there was no considerable extension of the process to the adjoining glands. Four of the cultures, all of which were from children, caused generalized disease in the cattle upon which they were inoculated. These cultures were so virulent for cattle that they were considered as having been originally bovine bacilli. As there were 16 cultures of tubercle bacilli from children tested, and 4 of these had the virulence for cattle of the bovine bacillus, it is evident that 25 per cent. of the cases of tuberculosis in children investigated by this commission were due to bovine infection, according to the test proposed by Koch. On the other hand, no bacilli were found among the 23 cultures obtained from adults which were virulent for cattle. The experiments made by this commission and by other investigators apparently settle the question of the transmission of bovine tuberculosis to children, and indicate that this occurs with considerable frequency, and that measures should be taken to guard against it.

Rabies.—Rabies is a contagious disease of dogs in which the saliva is virulent, and the contagion is communicated from animal to animal by biting. The human species, and nearly all species of animals, are susceptible to this disease and contract it when inoculated. The disease is not communicated otherwise than by direct inoculation.

This disease appears to have been known from the earliest historical times, and has been referred to with such detail as to manner of transmission and symptoms that there can be no doubt as to the identity of the disease with that which is now known under this name. There have been numerous cases recorded in which the disease spread among wolves, and these animals became so savage that they attacked human beings and caused many cases of rabies in man. Notwithstanding the length of time during which the disease has been described, there have been many who doubted its existence, and especially doubted its being communicated to the human subject. These people explain the deaths of persons following bites of rabid dogs by attributing them to nervous troubles produced by fear. Questions relative to the nature and identity of rabies were in much confusion until the subject was taken up by investigators and studied experimentally.

Zinke in 1804, and Count Salm-Reiferscheid in 1813, recorded successful experiments in the communication of rabies from animal to animal by inoculation. From 1836 to 1860 Renault and Rey in France made many successful inoculations, demonstrating that this was a specific disease, and that the period of incubation might vary from ten days to over one hundred days. Magendie, Earle, Hertwig, Renault, and others made successful inoculations from man to animals, proving that the human subjects were affected with this specific disease, and that the contagion could be reinoculated into animals, such as dogs and rabbits, and reproduce the disease in them. In Magendie's case the dog which was inoculated from the human subject was allowed to bite two other dogs, which in turn became rabid after forty days. It was consequently demonstrated that rabies is communicable to man as well as to animals, and that the saliva becomes virulent with man as it does with the lower animals. The value of rabbits for making the biological tests of rabies was pointed out by Galtier in 1879, and by Pasteur a few years later. The investigations of Pasteur (1881) showed the constant virulence of the brain and medulla, and that these organs, being protected from saprophytic germs, furnished a pure virus which might be used for biological tests. He also showed the value of the method of inoculating upon the surface of the brain, in which case the disease was transmitted with great certainty and the period of incubation was reduced to a minimum. This method of inoculation has been of much value to investigators in saving time and in making their results more accurate.

Notwithstanding the experimental demonstration that rabies is a specific disease and can be easily transmitted by inoculation from animal to animal or from man to animal, there are still physicians who express doubts as to the existence of the disease. Those who oppose the enforcement of measures for reducing or eradicating the disease in dogs support their position by quoting the sceptical opinions of such physicians, and are often able to counteract the efforts of sanitarians to lessen the evil. It has been alleged that disease with the symptoms of rabies could be produced in animals by inoculating them in the surface of the brain with various inert substances, and the conclusion was drawn from this that the disease produced when inoculating from brain to brain of supposedly rabid animals was a non-specific disorder of the nervous system. This rather far-fetched conclusion never had much foundation in fact, and has been completely disproved. It is impossible to produce a disease having the period of incubation and symptoms of rabies by inoculating with inert substances, and the disease which is produced in that manner is not communicable from animal to animal, neither is such disease accompanied by virulent saliva, nor can it be reproduced in dogs and cattle by inoculating subcutaneously with the saliva or with portions of the medulla, as can be readily done with rabies. The scientific demonstration of the existence of rabies as a specific disease is as complete as has been made in the case of any other disease, and it is decidedly unfortunate that so many physicians have failed to inform themselves of the details of these investigations. The general public look to physicians for reliable information on such questions, and when the opinions which

they receive are uncertain or even erroneous, great harm is done in preventing the adoption and enforcement of proper sanitary measures.

Symptoms of Rabies. The symptoms of rabies are such as we should expect to arise from a serious disease of the central organs of the nervous system. There are, first, irritation; second, paralysis and death. The rabies virus appears to have little effect upon the system until it reaches the brain and spinal cord, where it multiplies, causes irritation, and finally interrupts the functions.

Rabies in dogs is generally classified in two forms: First, furious rabies; second, dumb rabies. In the former the animal is irritable, aggressive, and bites nearly every object which comes in its way. In the latter, the muscles of its jaw are paralyzed almost from the first appearance of symptoms, and being unable to bite, it remains more quiet and tranquil. As a matter of fact there is no essential difference in these two forms of disease. The cases of dumb rabies are those in which the paralysis comes on early in the disease; but in all cases it appears sooner or later. The saliva from a case of dumb rabies is just as dangerous and virulent as that from a case of furious rabies. A dog does not necessarily bite everything which it comes in contact with, even when it has rabies and its jaws are not paralyzed. It may be aggressive and furious all of the time or only a part of the time, or not at all. There is no disease in which the symptoms vary more than in rabies of the dog, and it is consequently impossible in any description of moderate length to give an idea of the different forms under which it may appear.

Fleming has well said that it is a great and dangerous error to suppose that the disease commences with signs of raging madness, and that the earliest phase of the malady is ushered in with fury and destruction. The symptoms appear very gradually, and at first there is only the slightest evidence of brain disease. The animal's habits and behavior are changed. It may be more restless and affectionate than usual, seeking to be near its master or mistress, fawning or licking the hands and face, and apparently seeking for sympathy or assistance. Such caresses are, however, extremely dangerous, for it has been shown that the dog's saliva is virulent for a day or two before the appearance of any symptoms, and its tongue, moist with virulent saliva, coming in contact with a part where the skin is thin, abraded, or wounded, may fatally infect the person for whom the demonstrations of affection are made. The instances in which hydrophobia has developed from such inoculations are very numerous, and every one should be warned against this kiss of affection from a dog in the first stages of this disease, which carries with it not only death, but sufferings which are dreaded more than death itself.

In most cases dogs first become dull, gloomy, morose, taciturn, and seek solitude and isolation in quiet, sheltered places or under pieces of furniture. But even in this retirement they do not remain quiet. They are uneasy and agitated; they lie down and assume the attitude of repose, but in a few minutes are up again walking hither and thither, as has been said, "seeking rest but finding none." Sometimes this restlessness may disappear for a time and the animal becomes more lively and affectionate than usual. Often it sinks into a sullen gloominess from which even its master's voice arouses it but temporarily. It becomes more and more desperate in its efforts to prepare a comfortable bed, pawing or scattering the straw, or, if in a house, scratching, tumbling, and tearing cushions, rugs, curtains, carpets, and everything of that kind within its reach.

At this period dogs may have aberrations of the senses, of the sight, hearing, and feeling, which cause hallucinations and lead them to think that they are being annoyed by something, or that some animal or person is endeavoring to injure them. They crouch ready to spring upon an imaginary enemy, then rush forward and snap at the air; or they throw themselves howling and furious against a wall as though they heard sounds beyond it.

While at first the affected dog may not be disposed to bite, it becomes more dangerous as its hallucinations and delirium increase. The voice of the master or of an acquaintance may dispel the aberrations temporarily and lead to friendly demonstrations, but an unexpected movement or touch may bring on another access and lead to a quick and unexpected bite. The disturbance of the sensations leads to chills and itching. If the place where the bite occurred is accessible, the dog licks the scar and later bites and tears the tissues. This tearing of the flesh is not always confined to the site of the inoculation, but certain regions of the body appear to lose their sensitiveness, and at the same time to convey to the brain the sensation of itching. The animal in this case bites into its own flesh with apparent pleasure and satisfaction.

Such animals may take food until the disease is considerably advanced, if it is something which can be swallowed without mastication; otherwise it is dropped after remaining a short time in the mouth. Difficulty of swallowing is an early symptom, and frequently leads the unsuspecting owner to conclude that the animal has a bone in its throat. A dog which appears to have a bone in its throat is for this reason one of the most dangerous animals in existence. The supposed bone may be there, but on the other hand the symptoms which lead to this supposition may be due to partial paralysis caused by rabies, and the owner may be inoculated with the virulent saliva while thrusting his finger or hand in the dog's mouth to dislodge a bone which has no existence.

It is commonly believed that mad dogs have fear of water and are unable to drink, but this is incorrect. They differ in this respect entirely from the human patient. They have no fear or dread of water, but swim streams and continue to drink until paralysis has progressed so far that they are no longer able to swallow.

When the furious symptoms come on, a dog is inclined to leave his home and go upon a long chase, with no apparent object in view other than to be travelling onward. He trots at a rapid pace, eye haggard, tail depressed, indifferent to his surroundings. He flies at and bites dogs, other animals, and persons whom he meets, but usually does not apparently search for them or even notice them if they remain quiet. Dogs in this condition may travel many miles and finally drop from exhaustion and die. Often after an absence of a day or two they return to their homes, exhausted, emaciated, covered with dust, and presenting a forlorn and dejected appearance. Those who have pity for such an animal and try to make it clean and comfortable are in great danger of being bitten, for the disease has advanced to a point where delirium or aberration of mind is most marked, and where a treacherous bite is most common.

If the animal, instead of being allowed to escape, is kept confined, the paroxysms of fury are seen to appear intermittently, or, in the absence of provocation, they may be entirely wanting. When excited, it howls, rushes upon objects that are thrust toward it, or throws itself upon the bars of its cage and bites with great fury.

As death approaches, the animal becomes exhausted and scarcely able to stand; the eyes are dull and sunken, and the expression is that of suffering and despair. Paralysis appears in the jaws or in the posterior extremities, and extends rapidly to other parts of the body. The animal, being unable to stand, lies extended upon its side; the respiration becomes more and more difficult; there are spasmodic contractions of certain groups of muscles, complete prostration, and death. The ordinary course of the disease is four or five days. It may be as short as two or as long as ten days.

In a typical form of dumb rabies the disease comes on with restlessness, depression, a tendency to lick objects, and paralysis of the muscles which close the jaws. As a consequence of the paralysis, the lower jaw drops, the animal is unable to close the mouth, the tongue hangs out, and an abundance of saliva escapes. This condition has led to the erroneous conclusion that mad dogs always froth at the mouth. Later, the mucous membrane of the mouth becomes dry, discolored, and covered with dust.

The animal remains quiet, does not respond to provocations, and appears to understand its helplessness. As Bouley has said, the animal cannot bite and does not desire to bite. The course of the disease in this form is short, death usually occurring in from two to four days. This form of rabies is very common, and many persons know it as "drop jaw" who do not suspect its true nature.

Period of Incubation.—The incubation of rabies in persons or animals which have been bitten is extremely variable. Peuch has compiled a table of one hundred and forty-four cases of rabies in the dog, in which the date of inoculation and the appearance of the first symptoms were definitely ascertained. This table is reproduced from the "Nouveau Dictionnaire de Médecine, de Chirurgie et d'Hygiène Vetérinaire," and the writer has added a column of percentages.

INCUBATION OF RABIES IN THE DOG.

Number of days of incubation.	Number of cases.	Per cent.	Number of days of incubation.	Number of cases.	Per cent.
5 to 10	3	2.08	55 to 60	2	1.39
10 to 15	8	5.55	60 to 65	7	4.86
15 to 20	13	9.03	65 to 70	1	.69
20 to 25	25	17.36	70 to 75	5	3.47
25 to 30	13	9.03	80 to 90	7	4.86
30 to 35	25	17.36	100 to 120	4	2.78
35 to 40	6	4.17	365	1	.69
40 to 45	11	7.64			
45 to 50	9	6.25	Total	144	
50 to 55	4	2.78			

According to this table, the period of incubation may be less than ten days, or it may be as long as one year. Haubner mentions a case in which fourteen months elapsed after the bite before the disease appeared. Others have recorded cases in which the period of incubation was still longer.

It is plain, therefore, that when a dog has been bitten it cannot be safely allowed to roam at large after it has been isolated but a few weeks. For absolute safety, every dog bitten by a rabid animal should be destroyed, and no quarantine less than a year can be regarded as at all safe.

The Effect of Seasons upon the Development of Rabies.—The appearance of rabies is not confined to the hot months of summer, as is often supposed, nor to any other one period of the year. The writer has compiled a table of cases of rabies in dogs by months, which were recorded on good authority. This table covers 14,066 cases. The largest number of cases occurred in June, in which month there were 1,467. The smallest number of cases in any one month occurred in November, when there were 933. The number of cases in the other months varied between these two extremes. This shows clearly that there is no season of the year which is exempt.

The Prevalence of Rabies.—Rabies is a common disease of dogs in the United States. It has occurred continuously in the District of Columbia from 1895 to 1903, as shown by the investigations of the Bureau of Animal Industry. Reports have also been received of its existence in many parts of the United States, and particularly in the cities of New York, Philadelphia, Rochester, Buffalo, Chicago, Kansas City, Baltimore, and New Orleans. There have also been many reports of farm animals similarly affected in all parts of the country, but particularly in Virginia, West Virginia, Pennsylvania, Ohio, Indiana, Iowa, Nebraska, Kansas, and Minnesota. These various reports indicate that the disease is disseminated over the whole country, and that the losses of farm animals from it are considerable. It would also appear that a much greater number of persons are annually bitten than would be supposed from any pathological data which have been published.

Diagnosis of Rabies.—The symptoms of rabies in the first stages of the disease are not sufficiently definite to enable a positive diagnosis to be made, but there is a general rule which has been laid down by all who have had much experience with the disease, and that is that every dog whose habits and disposition appear to be suddenly changed should be considered suspicious and should be isolated. The development of rabies is so rapid that in the course of three or four days all doubts should be removed. If a person has been bitten by a suspected dog, the animal should be placed in a secure enclosure and held until a positive diagnosis can be made. This is extremely important, as it gives the infected person an opportunity to take the Pasteur treatment at a time when there is the best prospect of success. If a suspected dog has bitten some person and is afterward killed, the head and a part of the neck should be removed for subsequent investigation. A histological examination of the plexiform ganglion permits of an almost certain diagnosis being made. The presence of foreign bodies in the stomach is confirmatory evidence of rabies. To make the diagnosis absolutely positive, rabbits should be inoculated by the subdural method. As this latter method requires from two to three weeks for results to be obtained, the value of the diagnosis from examination of the plexiform ganglion becomes apparent. The writer's attention has been brought to one case in which the person bitten presented the first symptoms of rabies on the same day that the disease was diagnosed with the inoculated rabbits. If the diagnosis had been made by the rapid method, there would probably have been time for successful preventive treatment.

The Prevention of Rabies.—As rabies occurs in nature only from the bite of a rabid animal, it is sufficient to prevent such biting to guard against the appearance of the disease. While all kinds of animals may bite when suffering from rabies, it is almost always a dog which is responsible for causing the disease in man, and it is believed that cats generally contract the disease from being bitten by dogs. Efforts for prevention are therefore directed to the canine species.

The measure generally adopted is the destruction of worthless, ownerless, and vagrant dogs, but this measure cannot do more than reduce the disease without preventing it entirely. The most efficient measure for preventing the spread of rabies is to cause the dogs to be muzzled or led with a leash whenever they are allowed to appear upon the streets or in public places. This measure, if rigidly enforced, will soon diminish the prevalence of the disease, and, if enforced for a sufficient time, will eradicate it entirely. The success of Germany, Holland, Great Britain, and other countries with this disease by rigid muzzling has been remarkable, and demonstrates that the same plan can be relied upon wherever it is properly carried out. Vigorous objections are made to muzzling by the owners of dogs, on the ground that muzzles are inconvenient and irritate the animals. A properly fitted muzzle, however, is not uncomfortable, nor does it interfere seriously with the dog, except to prevent his biting. The objections to muzzling regulations when rabies exists in a community are therefore unreasonable, and should neither be urged by good citizens nor encouraged by sanitary officers. If persons insist upon keeping animals which are subject to a disease which may be communicated to human beings and cause such terrible sufferings with absolute certainty of early death as follows infection with rabies, they should be willing to adopt any measures that are necessary for the protection of the community.

ANTHRAX.—Anthrax, a disease known by the French and in some parts of this country as charbon, is a disease which affects most species of warm-blooded animals, and is widely distributed, apparently occurring in all parts of the world. It is most frequent in alluvial valleys which are subject to inundations. In the United States it is most common in the southern portion of the Mississippi valley. It has been reported from many other localities, however, in the Northern States as well as in the Southern, and on the Pacific coast as well as on the Atlantic seaboard.

Anthrax is caused by the *Bacillus anthracis*, an organ-

ism which appears to be able to multiply in nature outside of the animal body under certain favorable conditions. It is a bacillus which forms spores, and in that condition it is killed only with difficulty by heat and disinfectants, and is able to retain its vitality for years in the soil. It is consequently one of the most persistent forms of contagion, and pastures once infected may be said to be permanently dangerous.

The disease is seen most frequently in cattle and sheep, animals which are very susceptible to it; but it also occurs in horses and mules and in rare instances in swine. It may begin as a local swelling on some portion of the surface of the body, or the infection may enter the body in such a manner that internal anthrax, or anthrax fever, results. In the case of external anthrax, a small, warm, and painful swelling develops—usually on the shoulder, the neck, the throat, or about the head, under the belly, or at some other point—which rapidly enlarges and very soon becomes of considerable size. If incised, a small quantity of colored serum escapes, and fibrinous clots form, having the appearance of yellow gelatinous masses. General symptoms soon appear, and the disease rapidly progresses to a fatal termination, or in some cases there is improvement and the animal recovers in the course of one or two weeks. With anthrax that has no external tumors there are only the symptoms of intense fever with rapid loss of strength, and death in the course of two or three days. Very often the disease is so violent in its manifestations that the animals die within ten or twelve hours. Sometimes they die very suddenly without presenting any marked symptoms.

Post-mortem Appearances.—The carcasses decompose rapidly, the abdomen being distended with gas a few minutes after death. The subcutaneous blood-vessels are distended with blood, and the connective tissue and muscles are stained with hemorrhages of various sizes. Blood and reddish serum escape into the connective tissue and into the cavities of the body. A fibrinous exudate colored with blood is often found in the connective tissue, in the abdominal cavity, and sometimes in the lumen of the intestines. The glands are enlarged, softened, and deeply colored. Ecchymoses on the serous surfaces are common. The liver is generally congested and friable and often of a yellowish color. The spleen is remarkable for its size, being five or six times as large as usual, and is softened, more or less broken down, and engorged with blood.

Diagnosis.—The points by which a diagnosis is made in anthrax are, the existence of the animals in an area known to be infected with anthrax, the rapid development of the disease and the violence of the symptoms, the dark color of the tissues after death, the gelatinous exudates, ecchymoses, and especially the enlarged, engorged, and broken-down condition of the spleen. A microscopic examination of the blood after the death of the animal shows the presence of the Bacillus anthracis. In case of doubt the inoculation of a rabbit or a guinea-pig may be resorted to. The death of these animals in from twelve to forty-eight hours with the Bacillus anthracis in the blood enables a positive diagnosis to be made.

Anthrax and the Public Health.—Anthrax is a disease very easily communicated to man, and is frequently fatal in its effects. It has often been known as malignant pustule, or wool-sorters' disease. While anthrax is not communicated except by direct inoculation, the contagion is so active that such inoculation readily occurs. Men who handle the carcasses of the dead animals, especially if they try to save the skins or the wool, are particularly exposed to inoculation. Flies which have fed upon the blood of the dead animals may carry a sufficient quantity upon their proboscides to inoculate persons whom they afterward bite. Infected wool, hair, and hides are, however, the principal sources of the contagion with man.

To prevent the communication of the disease from animals to the human subject vigorous efforts should be made to stamp out the disease on its first appearance. The carcasses of animals which die should be burned or deeply buried, being covered with quicklime. If the infection is from a circumscribed area, all animals should be removed from this to healthy pastures. Great care should be taken in moving the carcasses to the places where they are to be buried. All blood which has escaped from the body should be carefully removed, and the ground upon which the body has lain should be disinfected by burning. In working with wool and hair precautions should be taken to avoid so far as possible the inhalation of dust, and if suspicious swellings develop upon workmen who handle animal products they should receive prompt medical treatment.

Animals affected with anthrax generally present such evident symptoms of disease and die in such a short time that the carcasses very seldom go upon the market for food. However, there have been cases in which meat affected with anthrax has been sold and consumed, and in some cases it has caused many fatalities. The inspectors of meat should be on their guard and should carefully investigate all carcasses in which there are any appearances resembling those seen in this disease.

Prevention of Anthrax in Animals.—In some cases it is possible to prevent anthrax by keeping animals away from the infected pastures and by draining and cultivating such lands. In most cases the extension of the disease may be arrested by the prompt and proper disposal of the carcasses of the animals which die. In sections where the lands are extensively infected, vaccination with a properly prepared vaccine has been practised with considerable success.

Glanders.—Glanders is a contagious disease of the genus *Equus*, and is readily communicable to man. It is caused by the *Bacillus mallei*, and is characterized by the formation of nodules or tubercles, which degenerate into ulcers from which there is a characteristic discharge. It is a disease which, as seen in the horse, is generally chronic, with not very apparent symptoms and little fever.

Small nodules, from the size of a shot to that of a small pea, form in the mucous membranes of the respiratory tract. These may be seen just inside the wings of the nostrils or on the septum, and are easily detected. They are at first red and hard, but soon soften, become yellow, and break, giving rise to a small ulcer the size of the tubercle. This ulcer has a grayish bottom and ragged edges, and there is given off from it a viscous, oily discharge which is very characteristic of the disease. Glanders tubercles may also develop in the lungs and other internal organs.

Sometimes nodules appear on the under surface of the skin, which soften, discharge their contents, and are transformed into an irregular ulcer with ragged, overhanging edges. These often lead to irritation of the neighboring lymphatic vessels, which become swollen and indurated and appear as hard ridges which are hot and sensitive to the touch. These ulcers are seen most frequently on the lips and neck, the lower part of the shoulders, and the inside of the thighs, but they may occur on any part of the body. This form of glanders is called farcy. Farcy is sometimes looked upon as a milder disease than glanders, but it should be remembered that both are caused by the same contagion, and that the only difference is the organ in which the lesions are localized. The internal lesions characteristic of glanders, and the farcy ulcers, are often seen in the same animal.

In acute glanders there is a rapid development of tubercles in the respiratory tract, which rapidly degenerate into ulcers. There is an abundant discharge from the nostrils, with considerable fever and a cough which varies according to the location and character of the eruption. Swellings form over the surface of the body, rapidly followed by farcy buttons which break and form ulcers. Acute glanders is often fatal within a comparatively short time, although in some cases the symptoms subside and the disease takes on a chronic form. Chronic glanders may continue for months or even years. In most cases it results in death sooner or later, but occasionally animals improve and apparently recover. In these

so called recovered cases, however, the internal lesions usually remain and the animals continue to spread the contagion.

Diagnosis.—The clinical diagnosis of glanders is based upon the existence of the nodules and ulcers in the nostrils, upon the character of the discharge, and the existence of an enlarged, nodular gland beneath the jaw. In cases of doubt, guinea-pigs are inoculated, and these animals develop a specific orchitis which enables a diagnosis to be made.

In recent years the toxin produced by the culture of the *Bacillus mallei*, which is known as mallein, has been used as a test on the same principle that the tuberculin test is applied for the diagnosis of tuberculosis. It is injected subcutaneously, and if the horse is affected with glanders there is an elevation of the animal's temperature and also a large, sensitive swelling at the point of inoculation. Mallein has been found very useful in picking out those animals in an infected stable in which the disease has not progressed far enough to show characteristic symptoms, and those in which the lesions are internal and in which the general health of the animal is not affected.

Treatment.—For practical purposes glanders may be considered an incurable disease. The measures to be adopted for its eradication are the prompt destruction of the diseased animals as soon as a positive diagnosis can be made, and the thorough disinfection of the stables in which they have been kept and of all the articles, such as harness, buckets, curry combs, and brushes, which have come in contact with them. Glanders is a common and widely disseminated disease, and more energetic measures than have heretofore been enforced are needed for its suppression.

Glanders and the Public Health.—Glanders is communicable to man by direct inoculation or by particles of the discharge from a glandered horse coming in contact with the mucous membranes of the eye, nose, or mouth. Usually it is the persons who care for the glandered horses that become affected. Sometimes, however, persons who are passing a diseased horse at the time when it snorts or coughs may become infected by the virulent mucus lodging upon their mucous membranes or on the skin where there is an abraded surface. Cases are also known in which a wife has taken the disease from her husband, and in which persons who have acted as nurses have contracted the disease from a patient. In man it is a loathsome disease and one which usually ends in death. The disease can be guarded against only by reducing the number of glandered horses, and, in case of the disease in man, by taking suitable precautions to prevent the transfer of the contagion to those who care for the patient.

Tapeworms of Animals in Relation to the Public Health.—The larval stages of several tapeworms are found in the organs of the meat-producing animals. *Cysticercus bovis* occurs in cattle, and when eaten by man gives rise to the common tapeworm found in this country, known as *Tænia saginata*. This tapeworm is not a very dangerous parasite. It may bring about digestive troubles, and it is occasionally very difficult to expel, but as a rule we may say that the parasite is only of temporary importance, its effects passing off when the worm is expelled.

The *Cysticercus cellulosæ*, or larval form of *Tænia solium*, occurs in pork. When the infested pork is eaten the adult parasite develops in man. Physicians should distinguish between the two tapeworms mentioned, because *Tænia solium* is a very much more dangerous parasite than *Tænia saginata*. If a patient soils his hands with the microscopic eggs during defecation, or if he has reverse peristalsis of the intestines strong enough to carry one or more segments of the tapeworm into his stomach, he may be infected with the larval stage of *Tænia solium*. In this case the embryos escape from the segments to the stomach and wander to various parts of the body, more especially to the muscles, the eyes, and the brain. If one or more of the larvæ develop in the eye or in the brain, more or less serious conditions may result, according to the part which is affected. The physician, in treating patients affected with the *Tænia solium*, is also exposed to some danger of infection with the eggs, and such infection would produce the larval stage.

The existence of these two parasites in American cattle and hogs makes it proper to suggest that the practising physician has a duty to perform in seeing that all tapeworms passed by his patients are totally destroyed, unless they are preserved for scientific investigation. It too often happens that the patient is not properly instructed in this matter, and passes the worm in some place where the eggs are scattered so that they afterward infect animals. It has been observed that the meat inspection in Germany has resulted in decreasing the frequency of tapeworm disease in man, and also the infection with the larval stage of *Tænia solium*. We have no exact statistics on this subject in the United States, but it would appear that the meat-inspection system must necessarily contribute somewhat to the decrease of these parasites.

Another parasite of this kind is the echinococcus, which causes the hydatid disease. It is a bladder worm which may be found in almost any part of the body of the meat-producing animals, and especially in the lungs and liver of cattle, sheep, and swine. This parasite is not directly transmissible to man by eating an organ affected with the bladder worm, but if the hydatid is fed to a dog each separate head of the cyst—and there may be thousands in a single cyst—develops into a tapeworm, the *Tænia echinococcus*. This is probably the smallest tapeworm known, having very few segments, and only the last segment is gravid with eggs. The dog scatters the eggs of this tapeworm broadcast, and the domesticated animals become infected with it. Mankind may also become infected by too close intimacy with dogs. In Iceland, where men and dogs live during the long months of winter in the same huts and without any idea of sanitary precautions, it is said that one person out of forty-three is infected with the echinococcus disease. In some parts of Germany the disease is also very frequent. Post-mortem statistics have been given, showing that at Rostock 2.43 per cent. of the cadavers were affected; at Breslau, 1.47 per cent.; at Berlin, 0.76 per cent. The disease can be controlled only by careful meat inspection and the destruction of all hydatids that are found. To prevent the multiplication of this parasite dogs should be prevented from feeding upon the offal of slaughter-houses.

Daniel E. Salmon.

VEVEY, SWITZERLAND.—Vevey, situated on the northeastern shore of Lake Geneva, four miles west from Montreux, has an admirable position and a mild climate, but is less favorably situated than the latter resort in respect to protection from the north and northeast winds, and has a more changeable temperature. Its altitude is 1,250 feet above sea level. It is a town of about 8,000 inhabitants, and is renowned for its lovely views of lake and mountain, its charming walks and excursions, and its cleanliness. Some one has called it Dutch in cleanliness, French in gayety and love of pleasure, and Swiss in its sentiment. Together with the other towns in this protected region, it has been called the "Nice of Switzerland."

It is recommended as a favorable place for the "after-cure" to those who have been taking the waters at Aix-les-Bains, Vichy, Carlsbad, and other spas. It is also a good place for a residence before and after the Riviera season. Autumn is considered the best season, at which time one can take the grape cure, for a description of which the reader is referred to the article *Meran*, in Volume V. of this Handbook. In the summer the milk cure and lake baths are used.

The water supply comes from the mountains, and is said to be unexcelled. The mortality is very low.

In winter the mean temperature never goes below 32.5° F., and in summer rarely above 86° F. The average mean monthly temperature is as follows: January, 32.5° F.; February, 35° F.; March, 40.6° F.; April, 44.9° F.; May, 49.6° F.; June, 57.2° F.; July, 58.8° F.; August,

58.9° F.; September, 54.2° F.; October, 49° F.; November, 39.3° F.; December, 33.4° F. The yearly average is 46° F. The average number of rainy days for the year is sixty, and of snowy days, seven. Fog is rare. The "Bise" or cold north wind is often felt here and produces trying changes of temperature.

On account of the changeable temperature this resort is not to be recommended for pulmonary tuberculosis, but is favorable for convalescents, for persons suffering from general debility or from some nervous affection, for certain cases of digestive disturbances, and for those who for any reason are "run down." Higher latitudes can easily be reached by means of a funicular railway, and one can go from Vevey to the castle of Chillon by electric railway. Within easy distance of Vevey are very many walks and excursions through vineyards, parks, and gardens, affording extended and fine views. One also can make excursions on the lake, and there are boats for rowing. The accommodations are excellent, abundant, and not expensive; pensions abound. There are good physicians, and an English church.

Vevey is easily reached in about twenty-two hours from London, either by rail or by boat from Geneva, or from other points on the lake.

Lausanne, ten or fifteen miles farther west, possesses a climate somewhat similar to that of Vevey. It is cold in winter but sunny, and is exposed to the northerly and southwesterly winds. The town is hilly, and is 1,700 feet above sea-level. The especial features of this place are the inexpensive living and the excellent schools.

Of all these resorts on the northern shore of Lake Geneva, Montreux possesses the best climate and has the most protection from the north winds. *Vide Montreux* in Volume V. of this HANDBOOK.

In the Rhone Valley, to the eastward, are several resorts of value, such as Aigle-Les-Bains, a hydrotherapeutic establishment; Champrey; Sierre; and particularly Bex, beautifully situated in the midst of the mountains and possessing a mild climate. Spring and autumn are the best seasons. Here one can take the grape cure, and also employ the saline springs which are used in the form of baths and douches, excellent facilities for which are afforded at the Grand Hôtel des Salines. (See *Bex* in Vol. I. *Edward O. Otis.*

VIBURNUM OPULUS.—*Cramp Bark.* "The bark of *Viburnum Opulus* L. (fam. *Caprifoliaceæ*)," U. S. P. This is a large shrub growing in the northern parts of Europe, Asia, and America. It produces red fruits and in one of its cultivated forms is the snowball tree of our gardens. The bark is thus described in the Pharmacopœia:

"In flattish or curved bands, or occasionally in quills, sometimes 30 cm. long, and from 1 to 1.5 mm. thick; outer surface ash-gray, marked with scattered, somewhat transversely elongated warts of a brownish color, due to abrasion, and more or less marked with blackish dots, and chiefly in a longitudinal direction with black, irregular lines or thin ridges; underneath, the easily removed corky layer of a pale brownish or somewhat reddish-brown color; the inner surface dingy white or brownish; fracture tough, the tissue separating in layers; inodorous; taste somewhat astringent and bitter."

It is identical in composition and properties with the next, but is rather more frequently used for abdominal cramps. The dose is 4–8 c.c. (fl. ʒ i.–ij.), and it is commonly given in the form of the official fluid extract.

H. H. Rusby.

FIG. 5021. View of Vevey as seen from the Eastern End of the Lake of Geneva.

VIBURNUM PRUNIFOLIUM.—*Black Haw.* "The bark of *Viburnum prunifolium* L. (fam. *Caprifoliaceæ*)," U. S. P. This species is a shrub or small tree growing from Connecticut to Illinois and southward, with oval, obtuse or slightly pointed, finely serrated leaves, and sessile cymes of small white flowers. The stem-bark is in thin pieces or quills, glossy externally, of a purplish-brown color, with scattered warts and minute black dots; when

collected from old wood it is grayish-brown; the inner surface of the stem-bark is smooth and varies in color from white to a pale rust-brown; fracture, short; odor, peculiar, somewhat like that of valerian; taste astringent

FIG. 5022.—Flowering Branch of Viburnum Prunifolium. (One-third natural.)

and bitter. The root bark, which is very superior, is in small, chip-like, curved pieces, of a deep rust-brown and much more bitter.

It appears probable that a large part of this bark, especially that coming from the Southern States, is derived from one or two closely related species which have apparently the same properties.

Besides tannin and several organic salts, it contains the bitter glucoside *viburnin* and valerianic acid, the latter probably derived from the former. There is also some resin.

Viburnum is mildly diuretic and strongly antispasmodic, and is used almost wholly as a uterine sedative. This use is chiefly in the prevention of threatened miscarriage, for which it is one of the most generally useful drugs, but it also extends to other spasmodic and painful uterine conditions. The dose is 1–4 c.c. (fl. ʒ ¼–i.), and the official fluid extract is commonly employed.

H. H. Rusby

VICHY, FRANCE.—This far-famed resort, the most frequented in France if not in all Europe, is situated in the great central plain, on the right bank of the Allier River, at an elevation of about 750 feet above sea-level. It is easily reached from Paris, lying almost due south at a distance of about 230 miles. It has a permanent population of 12,000, augmented by from 50,000 to 60,000 visitors. In the season, which extends from May to October, it becomes a sort of second Paris in the character of its amusements and attractions. The climate is mild and much like that of Paris; during July and the first part August, however, the weather is often very hot. In the city there is a park with central garden containing the largest bath establishment in France; there is also a casino with a fine theatre, reading-rooms, etc. Indeed, every effort is made to render the resort most attractive to the visitor, as well as hygienically wholesome.

The waters are those known as thermal alkaline, different springs differing from one another chiefly in the temperature, which varies from 57° to 113° F., and in the amount of free carbonic acid gas. Some contain a very little iron. There are fourteen regular springs which constitute the principal group of the Vichy waters, and others in the neighborhood. The most important and best known of the Vichy waters are the Grande Grille, Célestins, Hôpital, Puits-Chomel, Lucas, Mesdames, Parc, Lardy, Puits-Carré, and Larband.

The following is the composition of the three first named of these springs according to Cyr in Jaccoud's "Noveau Dictionaire de Médecine et de Chirurgie Pratiques," given in grams per litre:

Solids	Grande Grille.	Célestins.	Hôpital.
Sodium bicarbonate	4.883	5.103	5.029
Potassium bicarbonate	.352	.315	.440
Magnesium bicarbonate	.303	.328	.200
Strontium bicarbonate	.003	.005	.005
Calcium bicarbonate	.434	.462	.570
Ferrous bicarbonate	.004	.004	.004
Manganous bicarbonate	Trace.	Trace.	Trace.
Sodium sulphate	.291	.291	.291
Sodium phosphate	.130	.091	.046
Sodium arsenate	.002	.002	.002
Sodium chloride	Trace.	Trace.	Trace.
Sodium chloride	.534	.534	.518
Silica	.070	.060	.050
Total solids	7.006	7.195	7.155
Temperature (Fahrenheit)	105.6	57	86

The waters are used both for drinking and for baths. There are several large bathing establishments equipped with every hydrotherapeutic appliance: vapor baths, thermal mineral-water baths, douches, inhalations, douche massage, and carbonic-acid baths and douches. The water is clear, and the taste of the Grande Grille is not disagreeable. The waters are generally taken in small doses, 100–400 gm.—varying according to the individual and his malady—before meals. The waters of the different springs are not drunk indiscriminately, but each according to the malady: thus, for example, the Grande Grille is for hepatic troubles; the Célestins, for gout; and so on. It is well for the patient to consult one of the local physicians as to the kind of waters he should take and the method to be pursued in their use; and one is at no loss to find a medical adviser here, for there are said to be about a hundred.

The affections for which these waters are most frequently recommended are various dyspeptic conditions—the indigestion of chronic alcoholism, chronic catarrhal gastritis or enteritis in which there are no very acute symptoms; hepatic conditions—gall stones. "In the latter affection, the physicians at Vichy claim for the waters an absolutely curative power, asserting that they not only prevent the formation of gall stones, but even relieve the pain of an acute attack, restore the appetite, and cause the jaundice to disappear." Even when surgical interference is considered necessary, it is advised to try the waters before an operation, if one can delay without danger, and, if an operation has been performed, to follow it by a course of the waters. In gout, rheumatism, uric-acid diathesis and diabetes, these waters have been found to be beneficial. In certain pelvic disorders of women they are also said to be of value. At least one-half of all the patients who frequent this spa are said to be dyspeptics.

A course of these alkaline waters is somewhat severe, and one should possess a certain amount of constitutional vigor to take them with advantage. An after-cure in Switzerland or elsewhere in a tonic climate should follow the Vichy "cure."

The accommodations are excellent, and there is an English church service.

The waters are largely exported, and can be had in almost every civilized land. Artificial Vichy, a more or less perfect counterpart of the natural water, is likewise everywhere to be had.

For an extended account of Vichy, its various bath establishments, and indications for the use of its waters, the reader is referred to "Stations Hydro-Minérales, Climatériques et Maritimes de la France," Paris, 1900.

Edward O. Otis.

VICKSBURG, MISSISSIPPI.—This city, picturesquely situated on a high bluff overlooking the Mississippi River, is about equidistant from Memphis and New Orleans. It is not a health resort, but is mentioned here and a chart of its climate is given as illustrating the climate of the lower Mississippi valley. The city is the largest in the State, with a population of about fifteen thousand, and is commercially important. It is, however, best known historically from the important part which it played in the Civil War. Besides the attraction of its fine situation on the river, it is also worthy of a visit from the fact that it contains the largest national cemetery in the country—a sad and forcible reminder of the intense struggle that took place about it.

CLIMATE OF VICKSBURG, MISS., LAT. 32° 22′, LONG. 90° 53′. PERIOD OF OBSERVATION, TWELVE YEARS.

	Jan.	March.	May.	July.	Sept.	Nov.	Winter.	Year.
Temperature (Degrees Fahr.).								
Average or normal	48.4	59.1°	73.4°	83.8°	79.7°	60.2°	50.4°	65.6°
Mean of warmest	56.4	69.8	83.5	92.3	85.0	66.4		
Mean of coldest	40.7	51.9	64.2	73.2	66.1	46.8		
Average daily range	15.7	17.9	19.3	19.1	18.9	19.6		
Highest or maximum	80.0	85.0	95.0	100.0	98.0	84.5		
Lowest or minimum	10.0	27.0	46.0	62.0	48.0	23.0		
Humidity.								
Average relative	71.4%	64.4	67.2%	72%	71.9%	70.8%	69.5%	69.6%
Precipitation.								
Average in inches	5.27	6.83	5.18	4.0	4.06	6.5	15.76	60.09
Wind.—								
Prevailing direction	N.	S.	S.E.	S.W.	N.	S.E.	S.E.	S.E.
Average hourly velocity in miles	5.9	6.8	5.2	4.0	3.9	6.2	6.2	5.4
Weather.								
Av. No. clear days	6.9	10.2	12.6	10.0	12.0	9.5	23.1	122.6
Av. No. fair days	9.9	10.6	11.7	14.9	11.2	11.1	30.0	142.8
Av. No. clear and fair days	16.8	20.8	24.3	24.9	23.2	20.6	53.1	265.4

Referring to the table, the reader will observe that the climate is quite semi-tropical—mild in winter and hot during a long summer. There is a large amount of rain quite evenly scattered throughout the year, although rather more falls in the spring. Attention is called to the small wind velocity, there being considerably greater freedom from wind in this valley station than at New Orleans at the mouth of the river, and at various other coast stations at this latitude or lower. There is a fair amount of sunshine, although the number of clear and fair days in this portion of the "sunny South" only exceeds the number in Boston, for example, by twenty-eight, and New York by fourteen.

Attention is also called to the similarity of this climate to that of the region represented by Little Rock, Ark. In the latter there are the same freedom from wind, about the same rainfall, and almost identically the same number of clear and fair days. The yearly temperature is also quite similar, though somewhat lower. It may be added that the climate of this region, represented by Vicksburg, is regarded as a healthful one.

Edward O. Otis.

VICTORIA, AUSTRALIA.—It is hardly to be supposed that an invalid from any part of Europe, or of the United States, or of Canada, would seek residence in so remote a country as Australia, and yet it will be of interest to give a brief summary of the climate of this portion of that country, containing, as it does, the most populous city of Australia, Melbourne; for the traveller or the merchant may have occasion to visit this portion of the world, if the invalid does not, and it may be of service to him to know something of the climatic conditions he is to encounter.

Victoria exhibits, in its physical features, the three divisions or regions common to the whole island continent: a littoral region of sixty or more miles in breadth; a mountain range approximately parallel to the coast, or from one to five thousand feet in elevation; and beyond these mountains lies the great inland basin, the home and origin of the hot winds. Of the peculiarities of the climate of the great inland basin or plains, perhaps sufficient mention has been made under the article *Australia* in Volume I. of the HANDBOOK, and it will be sufficient to repeat here that the climate of these vast plains is characterized by heat and dryness. The summers are hot, the thermometer frequently rising to 110° F., but the dryness of the air makes the heat more endurable. The other seasons of the year are "delightful." "In winter there is a little morning frost, but the midday is always warm. Autumn and spring present an almost ideal perfection of climate" (Lindsay). This is the great sheep-grazing country, the home of the "squatter."

The highland or mountain region exhibits the characteristic climatic features of altitudes: the range runs across the whole breadth of the colony, is well wooded, and the higher portions are often covered with snow. The existence of this mountain range is the one topographical feature of the country, says Richards, demanding attention on the part of any one desiring to understand the chief cause for such local modifications as exist in the general climate of the colony.

Of the coast region the climate of Melbourne can be taken as fairly representative, as well as representing in

CLIMATE OF MELBOURNE, VICTORIA. LATITUDE, 37° 49′ S.; LONGITUDE, 9H. 39M. 54S. E.—PERIOD OF OBSERVATION, TWENTY-SIX YEARS.

	Jan.	March.	May.	July.	August.	Oct.	Nov.	Dec.	Year.
Temperature—Degrees Fahr.:—									
Average mean temperature	66.6°	63.8°	53.3°	47.8°	50.2°	57.0°	60.9°	63.7°	60.39°
Average maximum for period 1880-84	79.9	75.5	61.9	55.4	59.9	66.1	70.7	73.7	
Average minimum for period 1880-84	55.2	55.3	47.2	41.0	44.5	46.9	51.1	53.2	
Average daily range	24.7	20.2	14.7	14.4	15.4	19.2	19.6	20.5	
Highest or maximum	111.2	104.6	82.1	66.1	74.7	95.8	103.2	110.7	
Lowest or minimum	42.3	37.1	31.8	27.0	28.3	32.1	38.1	40.0	
Humidity									
Average mean relative	64%	68%	78%	80%	75%	70%	67%	64%	71%
Precipitation									
Average in inches	1.60	2.13	2.16	1.78	1.89	2.88	2.44	2.36	25.76
Wind—	S.	S.	N.	N.	N.	S.	S.	S.	N. S. W.
Prevailing direction	and S. W.	and S. E.	and N. E.	and N. E.	and N. E.	and S. W.	and S. W.	and S. W.	and S.
Average hourly velocity in miles (1867-83)	11.0	9.6	9.5	10.1	10.7	11.3	11.1	11.3	10.50
Weather—									
Average number days of rain	7	8	13	13	14	13	11	9	134
Percentage of cloudiness	53	52	64	64	61	60	59	55	58

a general way the climate of the whole colony, and a study of the chart of Melbourne, herewith given, will serve to demonstrate the leading climatic characteristics.

In the first place it is to be borne in mind that Australia is south of the equator, and, hence, the seasons are reversed from those in north latitude; their summer is our winter, and so on for the other seasons. Whereas the mean summer temperature is the same as that of middle Europe, it will be seen that it is subject to great variability. The hot winds blowing from the desert of central Australia produce sudden great elevations of temperature, rapidly followed by a fall produced by a change in the direction of the wind. These hot squalls, as they may be called, produced by the hot north winds, are accompanied by dust and by a very considerable fall in the humidity; indeed, the heat and dryness are so intense that on one occasion apples were literally roasted on the trees. The highest mean temperature occurs in January, and the lowest from the middle of July to the beginning of August.

The winter is usually characterized by frequent rains and high winds. Ice and frost infrequently occur at this season, and at Melbourne the temperature seldom falls much below the freezing point.

The autumn season (March, April, and May) is considered "the most genial and beautiful portion of the year"; the temperature is moderate, the north winds grow cooler, and vegetation, which has been withered by the summer's dryness and heat, bursts forth again as soon as the moisture returns.

The spring (September, October, and November) resembles in character the autumn; the weather is usually mild and even quite warm. Sometimes there is a large rainfall in October and November; or there may be considerable diminution of rain at the beginning of October, and in November the dry and even hot northerly winds may blow and parch the vegetation.

In brief, the climate of this region is characterized by high temperature and frequent dust storms, comparatively mild winters, and agreeable climatic conditions in spring and autumn.

Sudden and extreme variability of temperature is not uncommon, especially in summer. The rainfall varies largely in different seasons—from nineteen to thirty-two inches. The percentage of cloudiness appears to be pretty high, though in general cloudless sunshine is one of the features of the Australian climate. The wind velocity is considerable, and, as has been mentioned, the hot north wind of the summer is a veritable furnace blast.

Melbourne itself, a city of about 500,000 inhabitants, including its suburbs, lies at the head of Port Philip Bay, and is spread out over a large area. There are wide streets, numerous parks, squares, and gardens, and many fine public buildings. The number of suburban towns and the great expanse of the city are a striking feature of the place. Melbourne appears to be a healthy place of residence. In rural Victoria pulmonary tuberculosis is not very frequent, but in Melbourne, as in all large centres of population the world over, this disease is prevalent. In the coast region rheumatism and cardiac affections are said to be common. Malaria does not prevail in Australia. *Edward O. Otis.*

VICTORIA MINERAL SPRINGS.—Custer County, Nebraska.

POST-OFFICE.—New Helena. Hotel built recently.

New Helena is reached by the Burlington and Missouri Railroad. The springs are seven in number, and are at a level of 2,600 feet above tide water, in a level prairie country having fine roads. It is said that an average of three hundred and fifty clear, sunny days in the year may be counted upon in this region. The accommodations for visitors are limited at present, but improvements are at this time being added. The springs were discovered in 1888, and it is stated that no two of them are exactly alike. The largest, known as the "Magnesia" Spring, is used for bottling. Each spring has a different flow, yielding from twelve hundred to three thousand gallons per hour. An analysis, made in 1888, resulted as follows (we are unable to secure the name of the analyst): One United States gallon contains (solids): Calcium carbonate, gr. 15.63; magnesium carbonate, gr. 11.27; iron carbonate, gr. 0.08; sodium sulphate, gr. 2.16; calcium sulphate, gr. 18.03; magnesium sulphate, gr. 12.06; potassium sulphate, gr. 1.46; ammonium sulphate, gr. 0.23; sodium chloride, gr. 1.26; lithia, iodine, and bromine, traces. Total, 62.18 grains.

The water has an unvarying temperature of 55° F. It is coming into considerable use as a commercial water, and in addition to table and domestic use it is recommended for stomach and kidney disorders.

James K. Crook.

VICTORY STRONTIA SPA.—Put-in-Bay Island, Ohio. This mineral well is located on the spacious grounds of the palatial Hotel Victory, sixty miles by steamer on Lake Erie from Detroit, forty miles from Toledo, and twenty-two miles from Sandusky. The well is four hundred and ninety feet deep, and is sheathed with an iron casing for about two hundred feet. The water rises to a level of twenty-five feet from the ground surface and its supply appears to be practically inexhaustible. The following analysis was made by G. A. Kirchmaier, Ph.D., chemist to the Ohio Dairy Food Commission: One United States gallon contains (solids): Strontium sulphate, gr. 33.75; calcium sulphate, gr. 65.98; magnesium carbonate, gr. 14.35; calcium carbonate, gr. 25.69; iron, gr. 0.20; sodium chloride, gr. 1.12; potassium chloride, gr. 0.91; silica, gr. 0.14; alumina, gr. 0.08. Total solids, 142.22 grains.

This analysis is chiefly noteworthy on account of the large quantity of the comparatively rare ingredient of strontium which it exhibits. The therapeutical relations of this agent have not yet been fully outlined. Some of the salts of strontium have been found to possess a useful application in chronic gouty manifestations, in muscular and in subacute articular rheumatism, and in diabetes. More recently it has been employed with apparent advantage in parenchymatous nephritis. Some observers have recommended strontium as a valuable intestinal antiseptic, and useful in flatulent dyspepsia, with fermentative changes in the alimentary tract. Aside from the possession of this ingredient the waters of the Victory Spa would appear to possess useful properties as a mild saline laxative and antacid. The fortunate location of the well so near the big summer hotel, whose name it bears, will no doubt serve to bring it to speedy notice.

James K. Crook.

VILLACABRAS SPRINGS, SPAIN.—The springs of Villacabras are situated in the province of Madrid, Spain, and are owned by a French company which exports this water under the above name. It is a natural mineral purgative water, and is said to have neither a repulsive smell nor a bitter taste, and to be painless in its action.

The analysis, made by Prof. C. F Chandler, of New York, is as follows:

In one United States gallon there are (solids): Sulphate of soda, gr. 9,340.5765; sulphate of potash, traces; sulphate of magnesia, gr. 213.3164; sulphate of lime, gr. 119.0627; sulphates of iron and alumina, traces; chloride of sodium, gr. 50.9641; silica, gr. 2.2219. Total, 9,726.1416 grains.

As will be seen from the above, the "Glauber's salt" is the principal ingredient of this water, and the one upon which its purgative action depends. The dose is, as a laxative, from four or five tablespoonfuls; as a purgative, half a tumblerful or more. The effect of the water is said to be increased if it is diluted, and it is therefore recommended that in intervals between the doses some light liquid nourishment or plain water be taken.

Villacabras water can be recommended for those conditions which require a non-stimulating laxative or pur-

gative, such as hepatic torpor, chronic constipation, gastro-intestinal catarrh, etc. It is also recommended for children and persons of delicate taste on account of its freedom from objectional odor and bitter taste.

Edward O. Otis.

VIOFORM, iodochloroxychinoline, is an antiseptic powder recommended by Tavel, Bischler, and others as an efficient and odorless substitute for iodoform.

W. A. Bastedo.

VIRGIN HOT SPRINGS.—Washington County, Utah. Post-Office.—Washington. Visitors accommodated in ranches near by.

These springs are located on the Rio Virgin, four miles south of Togneryille. The nearest railroad station is at Milford, Beaver County, eighty miles distant, by private conveyance. The elevation here is 3,200 feet above the sea-level. The surrounding country is of a rugged, mountainous character. According to Mr. Thomas Judd, of St. George, Washington County, the rainfall does not exceed three and one-half inches annually. The air is mild, sweet, and balmy, even during the winter months. On February 27th, 1896, the date of Mr. Judd's letter, almond and apricot trees were in full bloom in the open air. The springs are six in number, and supply a stream large enough to run a grist mill. The temperature of the water is 130° F. No analysis has yet been made. The springs have not been much improved as yet, but are resorted to by the settlers for rheumatism, skin diseases, and other affections. It is the intention of the present owners to put the springs into proper shape as a health resort as soon as the railroad has been completed to within a reasonably accessible distance.

James K. Crook.

VIRGINIA BEACH, VA. See *Old Point Comfort.*

VIRGINIA HOT SPRINGS. See *Hot Springs, Bath County, Va.*

VISCERA, HOLLOW, AND BONY SINUSES, MEASUREMENTS OF.—The formation of a standard of measurements of the hollow viscera of the human subject is attended with the difficulty that the viscera themselves vary in size, even in the same individual at different times. A cavity or tube with soft, yielding, elastic, muscular walls, allowing expansion and contraction within wide limits, must be always changing in size with the changes in its solid, liquid, or gaseous contents. There cannot, therefore, be any fixed, determinate standard; but the size must be said to be *about* thus and so, varying not only with the conditions just stated but with the development of the individual. Any consideration of dilatations due to obstruction below, or of abnormal contractions due to disease of the part itself, is outside the scope of this article; but these variations illustrate well the degree which expansion or contraction may attain.

The basis of this article is mainly the work of previous investigators, supplemented by some of my own. In determining what should be considered hollow organs there was some difficulty, since all the vascular and mucous canals might be included. I decided to limit the article to the subjects mentioned below; and, at the suggestion of the editor, I have added the maxillary sinus. For measurements of the nose, mouth, heart, and womb and its appendages, I would refer to the special articles in this Handbook, and to monographs and text-books treating of those organs. Much valuable information is obtainable from Cruveilhier, Cloquet, Quain, Allen, Holden, Mackenzie, Todd and Bowman, and Richardson.

Measurements of diameters may be understood as including the walls of the cavity or canal, which are usually so thin as practically not materially to alter what, at the best, are variable results. In some cases, as in the investigations of Mackenzie on the œsophagus, plaster-of-Paris was run into the viscus and allowed to harden. The measurements were then taken upon the mould. Whatever material is used for filling or injection, it will, of course, be necessary to support the organ in water or other fluid, to prevent misshapement; I suspect that even then the best obtainable results would be only approximately correct.

The *pharynx* is a bag-like canal, closed above but continuous below with the œsophagus, communicating in front with the nose, fauces, and larynx, and lying at the back against the first five cervical vertebræ. Its œsophageal end is usually opposite the cricoid cartilage in front and the body of the fifth cervical vertebra behind. Its length and diameters vary according as the organ is in a state of rest, or as deglutition or speech is taking place.

It is subdivided into three portions: A nasal portion, or naso-pharynx; a buccal and guttural portion, or oro-pharynx; and the laryngo-pharynx. In the modulation of the voice the oro-pharynx is the part almost exclusively affected; in deglutition, movements of both oro- and laryngo-pharynx take place.

The length is usually stated to be from 4 to 4.5 in. (10 to 11.5 cm.) which may be increased to 5.5, or even 6.5 in. (14 to 16.5 cm.), by distention, or reduced to 2.5 in. (6.5 cm.) in the greatest possible contraction. Mackenzie gives the maximum length at about 5, and Allen at 5.5 in. (12.5 to 14 cm.). Allen gives the length of the naso-pharynx at 1.5 to 2 in. (4 to 5 cm.).

The breadth varies in different parts. The superior transverse diameter, measured between the posterior margins of the internal pterygoid plates, is, according to Mackenzie, 1.6 in. (4 cm.), to Cruveilhier, 1 in. (2.5 cm.), and to Allen, 8 lines (16 mm.). This diversity of measurements shows well the great variation in size in different subjects.

The diameter of the buccal portion, taken between the posterior extremities of the alveolar borders, is, according to Cruveilhier, about 2 in. (5 cm.), but may be reduced to 1 inch by the contraction of the constrictors.

The widest part of the laryngo-pharynx, opposite the greater cornua of the hyoid bone, measures 2 in. (5 cm.). Cruveilhier, however, measuring between the summits of the greater cornua, found but 1 in. and 2 lines (3 cm.); and between the superior cornua of the thyroid cartilage, 1 in. and 2 or 3 lines (3 cm.). [A comparison of hyoid bones from different adults has given me distances, between the summits of the greater cornua, varying from $1\frac{5}{16}$ in. (33 mm.) to $1\frac{10}{16}$ in. (41 mm.)].

The narrowest part, opposite the cricoid cartilage, is about 1 in. (2.5 cm.). Cruveilhier gives the breadth in the interval between the inferior cornua of the thyroid cartilage as about 11 or 12 lines (2.5 cm.); muscular contraction here may obliterate the cavity.

The antero-posterior diameter varies less than the vertical or transverse. It is increased when the larynx is carried upward and forward, and diminished when it is carried upward and backward; it may be said to depend generally on the length of the basilar process of the occipital bone. Mackenzie gives it as $\frac{4}{5}$ in. (20 mm.) for the naso-pharynx.

The *œsophagus* varies in length according to the stature of the individual. The canal extends from opposite the fifth cervical vertebra to the level of the tenth thoracic. In the adult male it is from 9 to 11 in. (23 to 28 cm.) in length.

The diameter varies at different levels. It is narrowest at the beginning, opposite the cricoid cartilage, and becomes narrowed also somewhat in passing through the diaphragm. Allen states that it is narrowed at the beginning of the thoracic portion, being there 1 in. (2.5 cm.) in diameter. Mouton and Mackenzie made elaborate measurements, which show, among other things, that the transverse diameter is much greater than the antero-posterior. A comparison shows the transverse diameter at the beginning of the canal to be from $\frac{4}{5}$ to 1 in. (21 to 25 mm.); 6 inches below this point, $\frac{3}{4}$ to $\frac{4}{5}$ in. (18 to 21 mm.). It then steadily increases until it reaches 1 in. (25 to 27 mm.). It is from $\frac{3}{5}$ to 1 in. (16 to 25 mm.) where the tube passes through the diaphragm, and then slightly increases.

The antero-posterior diameter at its origin is $\frac{2}{5}$ to $\frac{3}{5}$ in. (10 to 14 mm.); at one-third of its length below, $\frac{1}{2}$ to $\frac{3}{4}$ in. (12 to 19 mm.); at a point two-thirds of the way down, $\frac{3}{4}$ to $\frac{4}{5}$ in. (15 to 20 mm.); at the lower end, $\frac{1}{2}$ to 1 in. (14 to 25 mm.).

The method of examination is to fill the œsophagus with plaster-of-Paris and measure the mould.

The *stomach* is very mobile and distensible, is subject to prolonged distention, and may also contract much when empty. It is much larger in those who eat but one, and that a full, meal a day. In certain diseased conditions, as in stricture of the pylorus, it may become enormously distended. In long-continued abstinence it becomes much contracted. As the result of the action of strong acids, it is said to have contracted to the size of an ordinary gall bladder.

Its length, from the cardiac cul-de-sac to the pylorus, is from 9 to 12 in. (23 to 30 cm.); Todd gives it as from 13 to 15 in. (33 to 40.5 cm.). The widest diameter is between 4 and 5 in. (10 to 12.5 cm.); at the pylorus it measures 2 in. (5 cm.), and for the whole organ 4 in. (10 cm.). The total surface is about $1\frac{1}{4}$ square foot; capacity, about 175 cub. in. or 5 pints (2.5 litres); Allen estimates the capacity as 62 ounces. The greatest circumference is 13 in. (33 cm.); the smallest, 3 in. (7.5 cm.).

The *small intestine*. It is probably impossible to measure the length of the small intestine with anything more than an approach to accuracy, because of its convoluted shape. After the mesentery is cut away preliminary to the measurements the intestine becomes lengthened immediately on manipulation, so that the length is greater than it was before the section. The calibre, too, is very variable, according to the increase and decrease of gaseous and other contents. Its length is usually stated at 20 to 25 ft. (6 to 7.5 metres).

Its calibre gradually diminishes from the beginning to its point of junction with the large intestine. Some of the older anatomists, as Cruveilhier, stated incorrectly that the intestine was funnel-shaped. Sometimes, in obstruction of the bowel, it becomes enormously dilated; and at other times may be exceedingly contracted. When distended it is cylindrical; when empty it may be elliptical.

The *duodenum* extends, in the shape of a horseshoe, from the pyloric end of the stomach to the left side of the second lumbar vertebra, opposite the superior mesenteric artery and vein. It is named from its length, which is equal to the breadth of twelve fingers. Most authors give the length as from 10 to 12 in. (25 to 30 cm.); Cruveilhier and Richardson make it 8 or 9 in. (20 to 22.5 cm.). It may be subdivided into four portions. The first, the ascending or hepatic, extends horizontally backward and to the right, and joins the second portion near the neck of the gall bladder; it is about 2 in. (5 cm.) long. The second, or vertical portion, uniting at an angle with the first, descends vertically and a little toward the left, as far as the third lumbar vertebra. Its length is from 2 to 3 in. (5 to 7.5 cm.). The third, or lower transverse portion, directly continuous with the second, is the longest and narrowest of the three; its length being from 3 to 4 in. (7.5 to 10 cm.), or, according to Todd, 5 in. (12.5 cm.). The fourth or second ascending portion ascends vertically by the left side of the spine, and is 1 in. long, (2.5 cm.).

The calibre of the small intestine is $1\frac{1}{4}$ to 2 in. (3 to 5 cm.). My own measurements in the adult have given $1\frac{1}{8}$ to $1\frac{1}{4}$ in. (28 to 31 mm.), and in the new-born infant $\frac{1}{4}$ in. (6 mm.). The circumference, as measured by Cruveilhier, was from 5 to $6\frac{1}{2}$ in. (12.5 to 16 cm.) at the beginning of the small intestine, $4\frac{1}{2}$ in. (10.5 cm.) at the middle, $3\frac{1}{2}$ in. (nearly 9 cm.) a little above the ileo-colic valve, and $4\frac{1}{2}$ in. (11.5 cm.) at the valve itself.

The *large intestine*, after removal from the cadaver, may readily be measured along its tapes. Its length is from 4 to 6 ft. (1.2 to 1.8 metre). Distention is said to diminish the length.

Its diameter gradually diminishes from its beginning to the end, except that there is a considerable dilatation just above the anus. In a general way, it may be stated to be from $1\frac{1}{2}$ to $2\frac{3}{8}$ in. (3.5 to 7 cm.).

The measurements of the individual parts are as follows:

The *cæcum* is the largest part of the large intestine (it is small in the carnivora, large in the herbivora). Its length is three or four fingers' breadth, from 2 to 4 in. (5 to 10 cm.). Its diameter is about the same as the length. Cruveilhier made two measurements of its circumference, the cæcum being moderately distended; just below the ileo-colic valve it measured 11 in. and 3 lines (28.5 cm.); in another subject, $9\frac{1}{2}$ in. (16.5 cm.).

The *vermiform appendix* varies greatly in length, being from 1 to 6 in. (2.5 to 15 cm.). Its diameter is usually given as that of a crow quill or goose quill—about one-third of an inch (8 mm.). It is a little wider at the cæcal junction.

The *ascending colon* is about 8 in. long (20 cm.); the transverse colon, 12 in. (30 cm.); the descending colon, 11 in. (27.5 cm.); and the sigmoid flexure, 22 in. (56 cm.). Cloquet states that the transverse colon is longer and larger than the ascending and descending portions, which are about equal to each other. The diameter of the ascending portion is less than that of the cæcum, and greater than that of the transverse colon. The circumferences of the parts, according to Cruveilhier, are as follows: The ascending colon and right half of the arch, 8 in. 9 lines (22 cm.) in one subject, 5 in. (12.5 cm.) in another; of the left half of the arch and descending colon, 6 in. (15 cm.) in one, and $5\frac{1}{2}$ in. (14 cm.) in the other. The sigmoid flexure was $5\frac{1}{4}$ in. (13.5 cm.) in circumference. My own measurements give a diameter of from $1\frac{5}{8}$ in. (40 mm.) to $2\frac{1}{2}$ in. (6.5 cm.) for the ascending and transverse portions and sigmoid flexure, and $\frac{3}{4}$ inch (18 mm.) for the descending portion, which, in my experience, is generally collapsed. In the infant, at term, the diameter of the colon was 1 in. (2.5 cm.).

The *rectum* is from 6 to 8 in. long (15 to 20 cm.). The first portion, from opposite the sacro-iliac joint to the middle of the sacrum, is about 3 in. (7.5 cm.) long; the second portion, to the end of the coccyx, $2\frac{1}{2}$ to 3 in. (6.5 to 7.5 cm.); the third portion, 1 to $1\frac{1}{2}$ in. (2.5 to 4 cm.). Its diameter in the upper part is the same as that of the colon, gradually increasing downward and finally contracting suddenly. Quain says that the upper part is narrower than the sigmoid flexure. According to Cruveilhier the circumference is 3 in. (7.5 cm.); in the lower part, 4 to 5 in. (10 to 12.5 cm.).

The *gall bladder* is from 3 to 4 in. long (7.5 to 10 cm.); and its diameter, at the widest part, is from 1 to $1\frac{1}{2}$ in. (2.5 to 4 cm.); in the infant, at term, $\frac{1}{2}$ in. (12 mm.). Its capacity is $\frac{1}{2}$ to $1\frac{1}{2}$ ounce (48 c.c.); it varies very much, and in some diseases may amount to 6 ounces (192 c.c.).

The *ureter* measures 12 to 18 in. (30 to 45 cm.) in length. In diameter it is equal to a crow quill or goose quill; the most contracted portion is in the substance of the bladder.

The *urinary bladder* is of a somewhat pyramidal shape; in a fairly dilated condition it measures about 5 in. by 3 in. (12.5 by 7.5 cm.); and its capacity is about 1 pint (0.5 litre), or, according to Allen, from 6 to 13 ounces (0.2 to 0.4 litre).

The female bladder is broader transversely and more capacious than the male. This may be partly due to the fact that women are more influenced by the customs of society than are men; and it is broader, also, more often in women who have borne children. The bladder is said to be relatively larger before than after birth, and relatively smaller in children than in adults. This also may be due to habit.

The temperament, nature of diet, temperature of the air, and position of the body, all may affect the size of the bladder.

The *vagina* of the unimpregnated woman averages 4 in. (10 cm.) in length on the anterior wall and 5 to 6 in. (12.5 to 15 cm.) on the posterior wall; according to Allen, the tube is $2\frac{1}{2}$ in. (6.5 cm.) long, its posterior wall being

5 lines (12 mm.) longer than the anterior. The walls may be separated in the virgin about 1 in. (2.5 cm.).

The *larynx* is said to be one-third larger in the male adult than in the female. The average length of the vocal cords is, in the male, 7 lines or $\frac{5}{8}$ in. (14 mm.); in the female, 5 lines (10 mm.). The measurements in a number of male subjects did not vary the twelfth of an inch. In females the cords are about one-fourth shorter than in the male. The average length of the glottis is, in the male, 11 lines (23 mm.); in the female, 8 lines (16 mm.). The transverse diameter of the glottis is, in man, 3 to 4 lines (6 to 8 mm.); in woman, 2 to 3 lines (4 to 6 mm.). Mackenzie gives the diameter as $\frac{1}{2}$ in. (12 mm.); in boys it is much less.

The *trachea* extends from opposite the fifth cervical vertebra to the second or third thoracic. Its length is from 4 to 5 in. (10 to 12.5 cm.), varying with the elevation and depression of the larynx and the extension and flexion of the neck. There is a difference of from 2 to $2\frac{1}{2}$ in. (5 to 7.5 cm.) between full extension and extreme contraction, the contraction being limited by the contact of the rings.

Its diameter is directly related to the capacity of the lungs, and is greater in the male than in the female; it is about the same throughout its whole extent, varying according to age and individual peculiarities, and is from $\frac{3}{4}$ to 1 in. (18 to 25 mm.). In a man, aged about ninety, whose trachea I measured, it was wider in the middle (namely, $1\frac{1}{4}$ in. or 31 mm.) than above or below, where it was 1 in. (25 mm.); antero-posteriorly the upper part measured 1 in. (2.5 cm.), the lower part $\frac{3}{4}$ in. (18 mm.).

The *right bronchus* is about 1 in. long (2.5 cm.); the left, 2 in. (5 cm.). The right is much wider than the left, its diameter being nearly as great as that of the trachea itself. In one woman whose trachea I measured, the diameter was 10 lines (20 mm.); the right bronchus was 8, the left 5 lines (16 and 10 mm.).

The *maxillary sinus*, or *antrum of Highmore*, varies greatly in capacity; it is relatively small in the young and large in the old. In a number of skulls of adults I found it to vary on the two sides. From its irregular shape I made no attempt to take its diameters, but only its capacity, which I obtained by crowding raw cotton against its connecting foramina and filling the sinus with mercury. In many measurements the capacity was found to be from 10 to 12 c.c. (ʒ iiss. to iij.); in a few it was as low as 8.5 c.c., and in others as high as 15 c.c. (2.7 and 3.75 drachms).

The *external auditory meatus* consists of a bony and of a cartilaginous portion. According to some authors these are nearly equal in length; others, as Allen, state that the bony portion is twice the length of the other. The entire canal is about $\frac{3}{4}$ to $1\frac{1}{2}$ in. (18 to 37 mm.) in length, a little longer on the floor than on the roof, because of the oblique direction of the tympanic membrane, the anterior wall and floor extending 3 or 4 lines (6 to 8 mm.) farther inward.

The diameter varies very much. In some subjects the end of the little finger can be passed in for quite a distance; in others the canal will hardly admit a goose quill. It is not of equal diameter throughout, being narrowest about the middle, although Allen states that it is widest at the junction of the bony and cartilaginous portions. The external portion is flattened from before backward, so that the vertical diameter (nearly $\frac{1}{2}$ in. or 11 mm.) is nearly double the antero-posterior ($\frac{1}{4}$ in. or 6 mm.). The middle portion is more cylindrical. The internal portion is flattened from above downward, making the antero-posterior diameter ($\frac{3}{8}$ in. or 9 mm.) greater than the vertical ($\frac{1}{4}$ in. or 7 to 8 mm.).

The *tympanic cavity* communicates in front with the Eustachian tube, and behind with the mastoid cells. Its diameters are as follows: Antero-posterior, about $\frac{1}{2}$ in. (12 mm.); Toynbee says, $\frac{3}{4}$ in. (18 mm.); the transverse diameter varies, in different portions, from $\frac{1}{16}$ to $\frac{1}{2}$ in. (2 to 12 mm.), it is narrowest in the middle; the vertical diameter is $\frac{1}{4}$ to $\frac{1}{2}$ in. (6 to 12 mm.).

The *Eustachian tube* connects the tympanum with the pharynx. It consists of an osseous and a cartilaginous portion. The osseous portion varies very much in length, according to different observers, ranging from $\frac{1}{2}$ to 1 in. (12 to 25 mm.); Allen says 14 lines (about 28 mm.). The length of the cartilaginous portion is about 1 in. (25 mm.); total length of tube about $1\frac{1}{2}$ in. (37 mm.); Toynbee and Cruveilhier say 2 in. (50 mm.).

The pharyngeal orifice is wide and dilatable; elliptical in shape; about $\frac{1}{2}$ in. (12 mm.) in diameter. The remainder of the tube is so constricted that it barely admits an ordinary probe. Sappey gives its vertical diameters as follows: Tympanic orifice, 5 mm.; at osseo-cartilaginous junction, 3 mm.; in middle of tube, 4 to 5 mm.; at pharyngeal orifice, 6 to 8 mm. Transverse diameters: Middle of osseous portion, 3 mm.; osseo-cartilaginous junction, 1 to 2 mm.; middle of cartilaginous portion, 3 mm.; at pharyngeal orifice, 5 to 6 mm.

The *mastoid cells* vary very much in size in different individuals and at different ages, being always small in youth. In some individuals they occupy the entire interior of the bone behind the external auditory meatus for $1\frac{1}{2}$ in. (37 mm.) and have a vertical diameter of 2 in. (50 mm.). They are usually subdivided, and communicate anteriorly with the tympanic cavity.

The *nasal duct*, including the lachrymal sac, is about 1 in. long (25 mm.), the sac and duct proper being nearly equal in length, namely, about $\frac{1}{2}$ in. each (12 mm.). The duct proper is directed downward, backward, and a little outward; is rather ovoid in section; its diameter varies greatly and is smaller than that of the sac; it varies also on the two sides of the same individual. The upper part averages about $\frac{1}{8}$ in. (2 to 3 mm.); the lower part is about 0.5 mm. wider. Noyes found in one case that the duct on one side was round and $\frac{1}{8}$ in. (3 mm.) in diameter; on the other, oval, and $\frac{1}{4}$ in. (6 mm.) in diameter. The nasal terminus is somewhat dilated.

The *frontal sinuses* vary much in size in different individuals, and on the two sides of the same. They are always small in youth. The right and left are generally entirely separate, but sometimes communicate through a small opening. They are often subdivided into smaller cavities.

My own measurements of capacity gave the following results: The right, $\frac{1}{8}$ to $1\frac{1}{2}$ drachms ($1\frac{1}{8}$ to 6 c.c.); the left, $\frac{1}{8}$ to $\frac{1}{8}$ drachm ($1\frac{1}{8}$ to $4\frac{3}{8}$ c.c.). As showing the difference, sometimes, between the two sides, I found in one case that the left sinus was to the right as 70 to 95. Perhaps the best idea of the size which they sometimes attain is formed from the fact that the larvæ of insects, living centipedes, musket balls, etc., have been found in these sinuses. *Daniel S. Lamb.*

VISION, PHYSIOLOGY OF.—In order to read with profit a presentation of the physiology of vision one should be thoroughly conversant with the anatomy of the eye, with the general principles of refraction, and with the application of those principles to the dioptrics of the eye.

The reader is referred to the excellent articles of Dr. Baker and Dr. Gradle on the anatomy of the eye (Vol. IV., p. 63) and the dioptrics of the eye (Vol. IV., p. 83).

Vision comprises two distinct phases of activity: 1. *Optical*, in which phase the eye as an optical instrument focusses upon the retina images of objects. 2. *Sensory*, in which the sensorium is made conscious of the form and color of the image through the neuro-epithelial cells, rods and cones, and the two orders of sensory neurones.

A. Visual Optics: The Eye as an Optical Instrument.

Possessing a lens with an adjustable focal distance, a diaphragm with an adjustable aperture, a pigment lining for absorption of dispersed light, and a screen for the reception of the image, the eye must at once be recognized as a typical optical instrument. Used as it is for viewing distant objects whose image is infinitestimal compared with the object, the eye resembles a telescope. But the

adjustable diaphragm in front of the lens and the screen for the reception of the image are points which make it more strongly resemble the photographic camera.

All of the optical instruments consist of two distinct mechanisms: (1) *A refractive apparatus* for focussing the rays of light, (2) *a directive apparatus* for directing the axis of the instrument at the object whose image is to be viewed.

1. Visual Refraction: The Refractive Apparatus of the Eye.—Before entering upon the consideration of this topic it might be interesting to note that the mechanical and thermal stimuli of one's environment are quite unmodified preparatory to their stimulation of the sensory end-organs, and the pressures and tensions and temperature act directly upon the sense organs transmitted practically unmodified through the superficial layers of the cuticle. The chemical agents, however, which serve to stimulate the sensory nerves of smell and taste must enter into solution before the end-organs are stimulated. Furthermore, the vibrations of ponderable matter must be condensed and intensified by the transmitting apparatus of the ear before they can sufficiently stimulate the end-organs of hearing.

Finally, the vibrations of the imponderable, luminiferous ether can only be recognized as light by the primitive eye spots of the cœlenterates and echinoderms. Nature has, through the lapse of ages, evolved a visual sense organ which is able to recognize not only the difference between light and darkness, but also to perceive the form and color of distant objects. In order to accomplish this rays of light are focussed into a clearly defined image through the refractive apparatus of the eye.

(*a*) *Application of the Laws of Refraction to the Mammalian Eye.*—See *Eye, Dioptrics of*, by Gradle, Vol. IV.

(*b*) *The Optic Disc or Blind Spot.*—(1) *The location of the blind spot* may be determined as follows (Marriotte's experiment): On a white card make a black cross and a circle about three inches apart. Closing the left eye, hold the card vertically about ten inches from the right eye so as to bring the cross to the left side of the circle. Look steadily at the cross with the right eye, when both the cross and the circle will be seen. Gradually bring the card toward the eye, keeping the axis of vision fixed upon the cross. At a certain distance the circle will disappear, *i.e.*, when its image falls upon the entrance of the optic nerve. On bringing the card nearer, the circle reappears, the cross of course being visible all the time.

(2) *The outline of the blind spot* may be determined as follows: Make a cross on the centre of a sheet of white paper and place it on the table about 30 cm. from the cornea; close the left eye and look steadily at the cross with the right eye. Wrap a penholder in white paper, leaving only the tip of the pen point projecting; dip the latter in ink, or dip the point of a white feather in ink, and keeping the head steady and the axis of vision fixed, place the pen point near the cross and gradually move it to the right until the black becomes invisible. Mark this spot. Carry the blackened point still further outward until it becomes visible again. Mark this outer limit. These two points give the outer and inner limits of the blind spot. Begin again, moving the pencil first in an upward, then in a downward direction, in each case marking where the pencil becomes invisible. If this be done in several diameters an outline of the blind spot is obtained, even little prominences showing the retinal vessels being indicated.

(3) *The size of the optic disc* may be readily determined by using the formula given below. Let x equal the long axis of the disc to be determined; a, equal the long axis of the map, as measured; d, the distance from the nodal point to the sheet of white paper upon which the map of the white disc was drawn; f, equal the distance from the nodal point to the retina: Then $x : a :: f : d$ or $x = \frac{a.f}{d}$.

(*c*) *Accommodation.*—See *Eye, Dioptrics of*, by Gradle, Vol. IV.

(*d*) *Imperfections of the Refractive Apparatus of the Eye.*—It will be remembered that the sole function of the eye as a refractive apparatus is to focus rays from any object, near or far, upon the retina; that when the accommodative apparatus is at rest the image of an object 6 metres or more distant is formed upon the retina in the normal eye. The distance of the image depends, then, upon the focal distance, but the principal focal distance depends in turn upon the radius of curvature, the index of refraction, and the location on the optical axis of the elements of the dioptric system. In the nature of the case the index of refraction cannot change perceptibly. In the principal imperfections of the refractive apparatus of the eye the position of the elements of the dioptric system upon the optical axis is faulty. If the screen (retina) is too far back the rays will come to a focus before reaching the retina. The subject will attempt to correct the difficulty by bringing the object near to the eye, thus increasing the conjugate focal distance until the image falls upon the retina. This bringing of the object near to the eye is a sign of a condition of the eye, which has, in consequence, been called "*near-sightedness*," or *myopia*, and it may be corrected by placing before the eyes concave or divergent lenses which enable the subject to see distant objects.

The retina may be too close to the nodal point; that is, the eyeball may be flattened in the antero-posterior diameter. In that case rays of light from a distant object would not be brought to a focus by the time they reach the retina. The subject will attempt to correct the difficulty by bringing into action the accommodative apparatus of the eye, thus bringing the focus nearer to the nodal point until it falls upon the retina and the object is clearly seen. This condition is called "*far-sightedness*" or *hypermetropia*. The oculists correct it by placing before the eyes convex or convergent lenses which enable the subject to see distant objects without the help of accommodation.

The radius of curvature of the cornea may be different in different planes. If the radius is shorter in the horizontal than in the vertical plane the rays which lie in that plane will be focussed nearer to the nodal point than will those which lie in the vertical plane. It must be evident that the eye would, under such conditions, be quite unable to focus both horizontal and vertical lines at the same time. Bringing the object nearer does not relieve the subject; using the accommodation does not help the condition. It is held by some ophthalmologists, however, that a modified accommodative act may contract the ciliary muscles in one place more than in another and thus correct or at least partially correct the condition.

The most effective way of relieving the condition without artificial means is for the subject to bring the eyelids very close together, leaving only a narrow horizontal slit. In this way all of the rays are cut out except those in one plane, and if these do not fall upon the retina when the eye is at rest, the subject may bring the object nearer to the eye or may use the accommodation. This condition of the eye is called by the oculists *astigmatism*, and it is corrected by placing before the eyes plano-convex or plano-concave cylindrical lenses which change the curvature of the refracting surface in one plane only. It is only necessary to adjust the axis of the cylinder at such an angle as to increase the curvature in the plane where it is smallest (or decrease it through the use of plano-concave cylinders in the plane where it is greatest) to put the dioptric system into approximately perfect condition.

2. Visual Mechanics.—As the telescope or the camera must be provided with a directive apparatus by means of which the direction of its optical axis may be changed, so the eye is provided with an apparatus for changing the direction of the line of vision. In directing the vision from one point or object to another the axis of the eye is turned upward or downward, outward or inward, or is circumducted, in short, the axis of the eye has an absolutely universal motion within its limits.

(*a*) *Monocular Fixation.*—The term monocular fixation is used to designate the mechanical adjustment of the eye to bring the image of the object upon the macula lutea, the most sensitive portion of the retina. If one studies the movements of one eye (the other being shaded) he will find that it readily follows the movements of an object held in front of it, however quickly or through whatever angles or directions it may be moved by the observer. The directive apparatus of the eye consists of the six muscles described in the article on anatomy, moving the eye about three different axes of rotation:

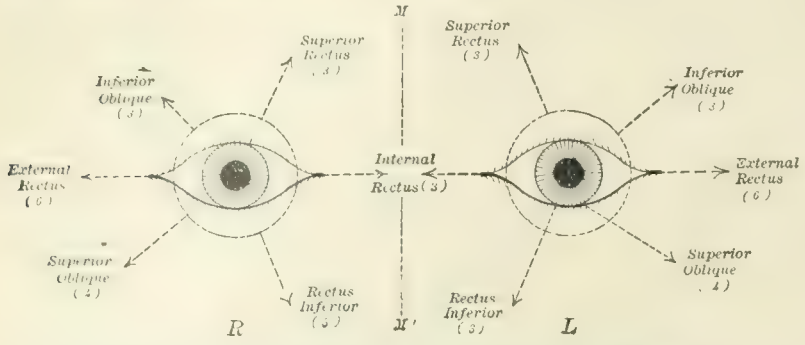

FIG. 5023.—Diagram to Illustrate the Directions toward which the Optical Axis is Directed or Inclined by the Contraction of the Individual Muscles. *MM'* is the median line; *R*, the right eye, and *L* the left one. The numbers in parenthesis (3, 4, and 6) indicate the innervation of the muscle. (After Waller.)

(1) A horizontal axis about which the eye rotates upward and downward; (2) a vertical axis about which the eye rotates from right to left; and (3) a longitudinal axis which coincides practically with the physiological axis or line of vision and about which the eye rotates (slightly) when the oblique muscles are in action. These three axes are rather arbitrarily located. Inasmuch as the eye is a spherical body resting in a hollow spherical socket, and inasmuch as it rotates freely in any direction about the intersection of the three assumed axes, it is somewhat simpler to take a central *point of rotation* about which the eye may rotate in any direction whatsoever under the action of one or more of its six muscles.

Waller's excellent diagram (Fig. 5023) given in the accompanying figure, will enable the student to interpret the mechanism of the directive power of the eye. Take, for example, the movement of the optical axis of the right eye outward or away from the median line in the horizontal plane. This movement is accomplished by the external rectus innervated by the sixth nerve. Again, take the movement of the axis of the eye upward in the vertical plane. It is evident that the superior rectus alone cannot accomplish this; but that that muscle must act in conjunction with the inferior oblique. In a similar manner movement vertically downward requires the combined action of the inferior rectus and the superior oblique.

In general the contraction of a single muscle causes a rotation of the eye in the direction indicated in the diagram for that muscle; while rotation in any other direction than the six which are indicated by the arrows requires the interaction of two muscles, and frequently the coördinative influence of two nerves. To circumduct the eye, sweeping its axis around a circle requires the action of all of the muscles, acting two or three at a time; an action the exactness of adjustment and the complexity of coördination of which must compel the admiration of any student of mechanics.

(*b*) *Binocular Fixation.*—This expression is used to designate the coördinated binocular movement which results in directing the physiological axes of both eyes upon the same object. If the object fixed by both eyes be a small one, its image falls upon the fovea centralis; if it be a large one, it will be disposed about that point symmetrically, as shown in Fig. 5024.

The lower part of the object being focussed upon the upper segment of the two retinæ, and the right part of the object being focussed upon the left part of the two retinæ, that is upon the median segment of the right retina and the external segment of the left retina.

It is evident that we have to deal with a complex mechanical action: (1) With double monocular fixation, and (2) with convergence of the visual axes of the eyes. If one refers to Waller's diagram he can readily tabulate the muscles involved in directing the two eyes in any particular direction. If in Fig. 5024 the object *O* move toward the right eye along the visual axis *ONF* the fixation of the right eye will not need to be readjusted. If, however, the visual axis of the left eye *ON'F'* follow the movement of the object, it will have to deflect to the right, thus making a greater angle ($< F$ *Om*) with the median line (*mm'*) than existed before. This increase of the *angle of convergence* is brought about by the internal rectus. If through weakness or through paralysis this muscle is unable to rotate the eye far enough to bring the points *O*, *N'*, and *F'* into a straight line, then the retinal image would not fall upon the field (*a'b'c'd'*) and there would be a double visual sensation, "double vision," or *diplopia*. Failure for any other reason to produce perfect binocular fixation leads to the same derangement of vision. This is the principal, though not especially frequent imperfection of the directive or mechanical apparatus of the organ of vision, and

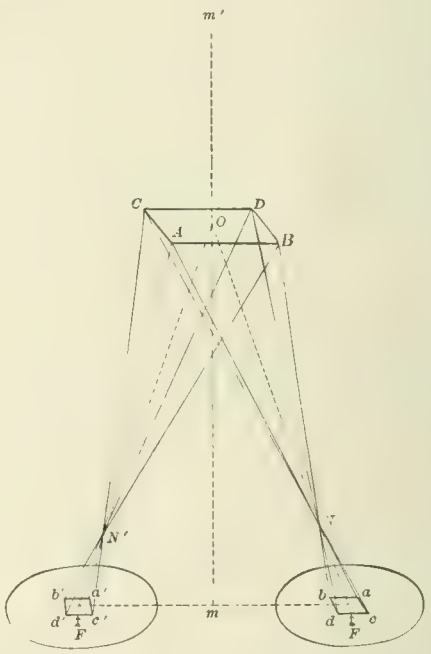

FIG. 5024.—Diagram showing the Symmetrical Correspondence of the Retinal Field. *N*, Nodal point; *F*, fovea centralis. The observer is supposed to be looking down upon the optical apparatus from above. Note that the line *C D*, which is on the lower side of the object, is the upper side of the image; and that the line *B D*, which is the right side of the object, is the left side of the image, which brings it at the inner segment of the right retina and the outer segment of the left retina.

is often corrected by oculists through the use of prismatic lenses which bend the optical axis, bringing the image upon the proper field of the retina.

B. Visual Sensation. The Eye as the Sense Organ of Vision.

The retina is the end-organ of vision; its function is to receive the impression of the image focussed upon its surface by the optical apparatus and to transmit the impression to the brain. About all that can be said is that the lights, shades, and colors of the retinal image excite, in the neuro-epithelial cells, metabolic changes which are influenced more or less by the action of the light upon the pigments in the associated tissues. The neuro-epithelial cells are composed of an efferent element represented by the cones or rods of the external layer of the retina that is the scene of the metabolic changes referred to above. The chemical changes start, along the afferent element (dendrite) toward the cell body, an impulse which is transmitted by the efferent element (neurite) to the first neurone of the cerebral layer of the retina, thence by the second neurone to the sensorium of the brain.

The phases of visual sensation which seem most profitable briefly to discuss are retinal stimulation, retinal irritability, and visual sensations.

I. Retinal Stimulation. *A. The Stimuli.—(a) The kinds of stimuli* which lead to visual sensation are limited normally to: (1) Diffuse light in its various colors, and (2) images of objects. In either case the stimulus is light, but it seems expedient in view of what is to follow to differentiate between the light in general and images of objects. The retina, in common with all highly specialized tissues, responds to all stimuli with the same general sensation. If one press upon the side of the eyeball a ring of light will be seen upon the opposite segment of the retina. The retina is stimulated under the finger, but it is referred to the opposite side. When a mechanical shock to the head makes one "see stars" these luminaries are real sensations due to the mechanical stimulus. Electricity may also produce the sensation of light.

Light being a mode of undulatory motion, it may vary in two ways: (1) In the number of vibrations per unit time, (2) in the amplitude of the vibrations. The first variation is comparable to the variation in the pitch of sound and leads to the color scale; the second variation is comparable to loudness, and is recognized in the intensity of the sensation.

(b) The duration of the stimulus may be very short. An electric spark whose duration is less than a millionth of a second is long enough to produce a sensation (Waller). The sensation which a stimulus calls forth is of much longer duration than the stimulus itself. This is made evident when one looks at a rapidly rotating wheel; a spoke occupies a particular position for only an infinitesimal fraction of time, yet it calls forth a sensation. In the position which the spoke takes during the next infinitesimal unit of time another sensation is induced; but the sensation of the previous stimulus persists and the two sensations blend. The result of this blending of the images of the rotating spokes is to produce the effect of a solid wheel. In a similar way if a luminous body be attached to the rim of the rotating wheel the sensation which it produces will not be a point of light, but a more or less elongated line of light. The faster the rotation of the wheel the longer the arc of light until finally the speed of the rotation may be great enough to extend the line of light around the whole circumference of the circle in a solid ring of light. Carpentier says that an interval of 0.027 of a second must elapse between two flashes of light in order that both can be seen separately.

B. The Irritability of the Retina.—1. *Factors Involved in Retinal Irritability.—(a) The structure of the retina* bears an important relation to its irritability. The two kinds of neuro-epithelial cells—the rods and the cones—are not equally distributed over the retina. There are no rods in the macula lutea; this portion of the retina possesses the cones only. The macula lutea is especially sensitive to the fine lines of images focussed upon it; *i.e.*, it is the only portion of the retina from which one may receive a clearly defined image. That portion of the retina outside of the macula lutea is only faintly sensitive to form, but is very sensitive to light and responds to very slight modifications in the intensity of the stimulus.

(b) The retinal pigments bear some relation to the irritability of the retina. Melanin or fuscin is the brownish-black pigment which makes up the pigment layer of the retina. This pigment seems to form a stock from which other pigments may be replenished. *Rhodopsin*, or "*visual purple*," is found in the rods, and is therefore absent from the macula lutea. *Chromophanes* are red, green, and yellow oil globules found in the cones. The chromophanes are not found in the eyes of mammals.

(c) Varying irritability of different areas of the retina is probably due to varying distribution of the rods, cones, and pigments. The following facts are important in this connection: 1. The macula lutea is the area of clearest definition of form; it is, in fact, the only area sensitive to the fine structural details of an image. 2. The macula lutea possesses cones but no rods, and in its most sensitive area—the fovea centralis—the cones are brought into special prominence by the thinning out of all the other elements. 3. The portion of the retina most sensitive to variations of the intensity of diffused light is that portion outside of the macula. 4. The portion of the retina outside of the macula is richly studded with *rods*, and each rod possesses its supply of rhodopsin. A solution of rhodopsin bleaches in the light. The retinal image may be acutally "fixed" by treating with four-per-cent. solution of potassium alum, the retina which has just been removed immediately after thorough exposure following rest in the darkness. The "fixed" image is called an *optogram*.

These facts seem to justify the conclusion that *the cones are the structures which receive form pictures, and the pigmented rods are the structures which receive light and color impressions.*

2. *Direct and Indirect Vision.*—These terms designate respectively the central field of clear definition and the surrounding field of indistinct definition. One may get a very good idea of the difference between direct and indirect vision by holding before one eye (the other being shaded) at a distance of 30 cm. a printed page. Direct the line of vision at a small word; the surrounding words will be recognized for a distance of perhaps 2 cm. in any direction, but by studying the sensation very carefully, keeping one particular letter constantly fixed in the line of vision, that one letter is the only letter upon the page that is absolutely clearly defined. The image of that letter lies upon the centre of the fovea centralis, the two adjacent letters lie upon the slanting sides of the fovea, their definition is only slightly less distinct than that of the central letter. The form of the next adjacent words can be made out with sufficient clearness to enable the observer to say definitely what the words are, but he would be quite unable to detect any slight typographical imperfection in the words. The field of direct vision may be taken to be that which is focussed upon the macula lutea which is 1.25 mm. in diameter, subtending about five degrees of angle at the nodal point.

(a) Indirect Monocular Vision. The field of indirect vision includes all of the visual field outside of that of direct vision. The accompanying figure (Fig. 5025) shows the field of indirect vision for white light bounded by the shaded portions of the figure. Note in the centre the five-degree circle of direct vision within which the form and structural features of objects are clearly defined. Note the blind spot (*B*) at the right of the macula in the figure, and showing that the optic nerve enters the eye to the median side of the fovea located from 12.5° to 17.5° from the centre and a little above the horizontal line from the fovea. Note that the boundary of the field for the indirect vision of the white light crosses the upper vertical meridian at 55°, the median meridian at 60°, the lower vertical meridian at 70°, and the external

meridian beyond 90°. The determination of the line bounding the field of vision is called *perimetry*, the record and the instrument used in getting it a *perimeter*. The field for yellow light is within that for white, the field

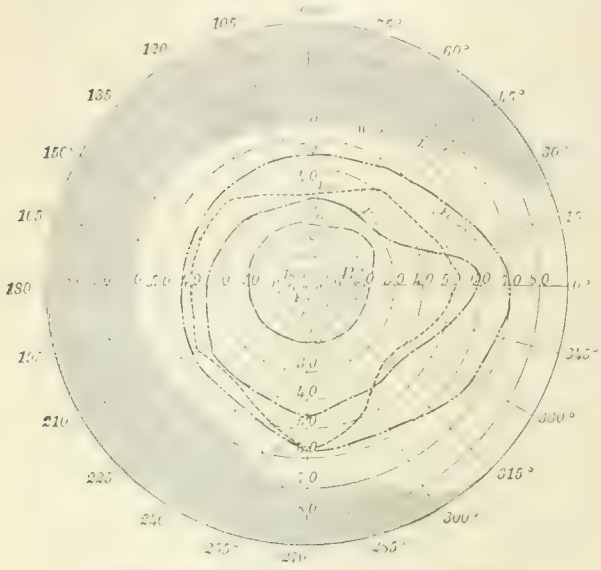

FIG. 5025. Perimeter Chart with Tracings. (Krapart.)

for blue light is within that for yellow, the field for red light still farther withdrawn from the periphery, and the field for green very much smaller than that for red. Perimetry has considerable clinical importance because in certain pathological conditions the perimeters are considerably modified either by being generally contracted or by being dotted with islands of total or partial blindness.

(*b*) *Indirect Binocular Vision.* To determine just what the field of indirect binocular vision is one has only to find the overlapping areas of indirect monocular vision when both eyes are directed to the same point. The accompanying figure (Fig. 5025) is for the right eye. If one trace upon the same chart the field sensitive to white light in the left eye, the open external end of the field will extend off to the left and the circular median end to the right, reaching the 60° circle. The right and left perimeters will thus overlap in an almost circular area bounded right and left by the 60° circle, above by the 55° circle, and below by the 70° circle. The field thus bounded is that for binocular indirect vision for white light.

II. VISUAL SENSATIONS.—(A.) *Fundamental Sensations.*—The sensations which light induces in the sensorium may not be so easily differentiated as are those of sound, but they are closely analogous to sound. In sound we differentiate pitch, loudness, and quality, dependent respectively upon number of vibrations per unit of time, upon the amplitude of the vibrations, and upon combinations of overtones; in light we differentiate *color*, *intensity*, and *form*, dependent respectively upon number of vibrations per unit of time, upon the amplitude of the vibrations, and upon combinations of intensities (lights and shadows).

1. *Form.* The sensation of detail in structure is clearest at the fovea centralis, and decreases progressively in every direction from that point in the retina. That this specialization of form-sensation is in some way connected with the fact that of the rods and cones cones only are present in the macula, and these are brought into special prominence in the fovea, has been suggested above. But the color sensation is also induced by stimulation of the fovea, though Kühne and others show that differentiation of color is less acute at the fovea than in areas outside of it.

2. *Intensity.* Intensity depends upon the amplitude of the vibration of the medium, which last transmits the light to the eye. As in the case of intensity of sound, this may depend upon the amplitude of vibration of the sonorous or the luminiferous body, or upon the summation of the effects of several vibrating bodies. The sound produced by two sonorous bodies of the same pitch and amplitude will be more intense because of the summation of the undulations; in the same way the light produced by two candles will be more intense than that produced by one.

The sensation induced by lights of varying intensity is not commensurate with the intensity, but obeys Weber's law of sensation: "The smallest change in the magnitude of a stimulus which one can appreciate through a change in one's sensation always bears the same proportion to the whole magnitude of the stimulus" (as formulated by Foster). Applied to vision, the proportion is 1 to 100, that is, 0.1 candle power added to or subtracted from a 10 candle-power light, 1 candle added to or subtracted from a 100 candle-power light, and 10 candles in a 1,000 candle-power light can be detected, and so on.

3. *Color.* Color depends upon the number of vibrations of a luminous body, as pitch depends upon the number of vibrations of a sonorous body. The white light that comes from the sun may be readily decomposed into a number of principal colors and an innumerable number of intermediate mixtures. The principal colors have the following rate of vibration: Red, 392 trillions of vibrations per second; orange, 532 trillions; yellow, 563 trillions; green, 607 trillions; blue, 653 trillions; indigo, 676 trillions; violet, 757 trillions. These vibrations range in wave lengths from 0.00000766 mm. to about half of that length.

The colors named above are the principal or the clearly pronounced colors of the spectrum. From three of these all other colors may be produced; these three are the fundamental or *primary colors: red, green, violet.* The accompanying figure (Fig. 5026) shows graphically the relation which these colors bear to each other. Not only does a combination of all of the colors produce white, but a combination of certain of the colors in pairs produces white; these pairs are called complementary colors: (1) Red and greenish-blue; (2) yellow and indigo; (3) orange and cyan blue; (4) violet and greenish-yellow.

How the different colors can stimulate the retina has been the subject of considerable controversy.

(*a*) *The Young-Helmholtz theory* assumes that there are in the retina three different kinds of sensory elements

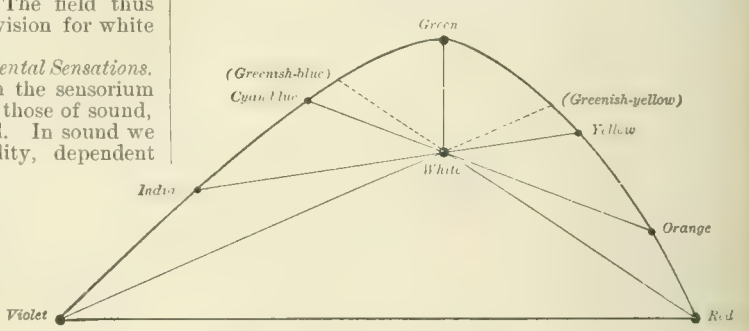

FIG. 5026. Geometrical Color Table.

which respond to the three different primary colors—red, green, and violet—and that "*every color of the spectrum excites all of the elements, some of them feebly, others strongly*" (Landois). The perception of color is then a resultant of the combined sensations brought to the sensorium by the three sets of elements.

(*b*) *The Hering theory* is based upon the principles of metabolism and upon the color law of Grassman. "If two simple but non-complementary spectral colors be mixed with each other they give rise to the color sensation, which may be represented by a color lying in the spectrum between both and mixed with a certain quantity of white"; *i.e.*, every color sensation except those of the primary colors may be produced by a color of the spectrum plus white. Hering assumes: (1) That light produces metabolism in the retina; (2) that the metabolic processes are in part anabolic and in part katabolic; (3) that white, red, and yellow sensations are katabolic, *i.e.*, accompanied by disintegration and fatigue; and that black, green, and blue sensations are anabolic, *i.e.*, accompanied by integration and rest; (4) these metabolic processes are assumed to be paired—*i.e.*, white and black sensations affect the same visual substance in opposite directions. Red and green stimulate another visual substance, and yellow and blue stimulate a third. Now, according to Grassman's law of color sensation: Any color sensation, except that of a primary color, may be produced by a color of the spectrum plus white. Hering assumes that white visual substance is katabolized not only when one sees white, but incidentally in all color sensations except primary ones.

(*c*) *The Franklin theory* is not antagonistic to either of the foregoing, but rather supplementary. It is based upon the facts of comparative physiology, and assumes that the rudimentary eye distinguishes between light and dark only, and possesses neither form nor color senses; so that the fundamental point of departure is a sensation of simple light or dark (Hering's white and black sensation) produced by stimulation of a fundamental "*visual gray*," which causes an accentuation of either the white or the black in it (presumably by modifications in the metabolism set up). This theory assumes that the yellow-blue substance was next developed and the red-green last.

The adherents of either the Young-Helmholtz or the Hering theory, especially the latter, may well accept the Franklin theory as supplementary, as it accounts easily for the fact that red-green color-blindness is most common, and yellow-blue blindness rather rare, while inability to see black and white is found only in cases of congenital, total blindness. Furthermore, reference to the perimeter chart shows that white-black covers the largest area of the retina, yellow-blue an area within that, while red-green is smallest and quite near the centre.

B. Secondary Sensations.—1. *After-images.* If one fix the gaze upon a brightly illuminated figure or pattern for fifteen seconds and then direct it toward a plain surface the image of the pattern gazed at will be seen upon the plain background of the second field of vision. If the after-image has the same colors as the first it is called a *positive after-image.* Positive after-images are usually caused by strong stimuli of short duration rather than by moderate stimuli of long duration. If the after-image is in the complementary color of the original pattern it is called a *negative after-image.* If one gaze intently at a green pattern, then turn to a red field, the pattern appears deep red upon the red field. It will also appear red upon a neutral field. *Negative after-images are a sign of retinal fatigue.*

2. *Contrast.* Contrast is the accentuation of a color sensation through contiguity or succession of another color, especially a complementary color. A piece of note paper may look white upon a black background, but if it is put upon a really white background it will be seen to be far from white. In a similar manner blue or yellow accentuate each other, as do red and green. Various other combinations have this reciprocal effect. If the effect is produced by looking at the two contrasting colors at the same time, the sensation is called *simultaneous contrast;* if by looking at the contrasting colors one after another, it is called *successive contrast.*

C. Color-blindness.—Of the male population four per cent. or five per cent., and of the female population about one per cent. are unable to differentiate certain colors. Such persons are called "color-blind."

1. *Complete Color-blindness* (*Achromatopsy*). Individuals thus afflicted can distinguish lights and shades, but have no color sense whatever. According to the Hering theory, they lack both the red-green and the yellow-blue visual substance; according to the Franklin theory they represent cases of arrested development of color sense in a condition representing a very primitive condition when only the fundamental color substance is present.

2. *Yellow-blue Blindness.* In this condition the blue end of the spectrum is absolutely dark, and the yellow may be more or less *illuminated*, but void of *color.* This represents also an arrest of development; but this arrest occurs after considerable progress has been made.

3. *Red-green Blindness.* This is by far the most common form of color-blindness, and as assumed by the Franklin theory to represent the last step in the development of the color sense and, therefore the first to fail in case of an arrest of development.

4. *Acquired Color-blindness* may result from disease of the retina.

5. *Normal Color-blindness* exists in the periphery of the retina. Passing from without inward the outermost sensation is that of white (and black); the next that of yellow and blue, followed by red and green (see *Perimetry*, on page 244).

III. Visual Perceptions and Judgments.—One may have a sensation of black lines upon a white surface without perceiving in the lines a letter or word. The retino-cerebral apparatus brings to the sensorium of the untutored savage the same sensations as it does to the sensorium of the scholar. The savage "senses" a written word upon a page, but does not *perceive* it; on the other hand, the scholar may "sense" the twigs upon the forest path without perceiving in their position and condition the track of an animal. Simple sensation involves nothing higher than the sensorium. There is no reason to believe that the sensorium brings to the consciousness of different individuals different sensations. Perception involves cerebration in the interpretation of sensations. Perception involves previous knowledge or memory of the same or related sensations. Effectual perception, like effectual marksmanship, depends upon the man behind the instrument.

Visual perception is the *seeing with understanding. Visual judgments* are based upon visual perceptions and represent conclusions reached after comparison of previous perceptions.

(*a*) *Acuteness of Vision.*—It is frequently necessary to test the acuteness of vision through a comparison of visual perceptions. An individual whose acuteness of vision is in question presents himself to the ophthalmologist for examination. If the subject is schooled in interpreting dim and distorted images, he may mislead the observer for a few moments with his acute perception, but the faulty sensation must sooner or later reveal itself. The observer will present to the subject a series of letters in unusual combinations, so that there will be no way in which he can get a clew for his judgment to work upon.

To be more concrete: The acuteness of vision is tested by reading letters of various heights at various distances. The normal eye (emmetropic eye) should see clearly at 6 metres—the oculists' infinity—letters which subtend an angle of 5′; *i.e.*, letters 1⅛ cm. in height. At 12 metres the normal eye should distinguish and name letters which are 2⅛ cm. in height. These letters subtend an angle of 5′—the minimum angle of clear vision. If the individual can see at 6 metres what he should see at 12 metres, he is credited with: Vision $= \frac{6}{12}$; if he can see at 6 metres what he should see at 30 metres, he is credited with: Vision $= \frac{6}{30}$. If by cultivation the visual power has been brought up above the average so that he can see at 6 metres what the average eye must bring to 3 metres to see, he will be credited with: Vision $= \frac{6}{3}$.

The acuteness of vision varies much with the habits and employment of the individual. Persons employed at fine close work acquire a microscopic vision—*i.e.*, ability to see and interpret the minutest detail of structure. Persons employed in vocations which require

long distance vision as acute as in simple eyes—i.e., ability to see and interpret small retinal images as objects. Sailors and engineers possess this ability to a marked degree.

[illegible] This [illegible] at least two [illegible] of sensation of the accommodative [illegible] the image of the object upon the [illegible] the converging [illegible] the [illegible] of the same object in the binocular vision. These sensations are examples of muscular sense. One estimates these muscular efforts instinctively. Upon these instinctive estimates one bases his judgment of the distance of an object. But other considerations may enter in to assist in the estimate of distance. For example, a movement of the head or body causes the [illegible] objects in the background [illegible] to move more rapidly than those [illegible] objects. One learns by experience how many [illegible] movement should be given [illegible] and how to [illegible] judgment accordingly. The known size of an object is an important factor in the estimate of its distance. In this estimate one instinctively measures the image and compares it with the image [illegible] at a given distance.

2. [illegible] This judgment is based upon two [illegible] The size of the image and (2) the distance of the object. Various other considerations may enter in to modify the judgment.

The subject of visual illusions belongs more properly [illegible] and will, therefore, not be considered here. [illegible] p. 1].

VITAL STATISTICS.—Vital statistics constitute the science of numbers as applied to the life history of communities. [illegible] The French term "démographie" is nearly synonymous with vital statistics. One of the highest living authorities (Körösi) defines vital statistics as [illegible] of the physical life of human society.

The principal data with which vital statistics are concerned [illegible] (1) Population, (2) marriages, (3) births, (4) deaths.

The significance or value of vital statistics lies very largely in the [illegible] these data to each other and to the various [illegible] with which they are usually classified: namely, the sexes, ages, conjugal condition, residence, occupation, race, season of the year, and, in the case of deaths and sickness, the cause of the same.

In the following paper upon vital statistics the writer has [illegible] of the data which were obtainable from the New England States and especially from the State of Massachusetts, since these States constitute [illegible] groups of States in the Union which have had a fairly complete system of registration during a period of several years. Maine being the last one of the New England States to adopt a system of registration [illegible] up to 1892.

[illegible] to the vital statistics of other States and countries as occasion requires.

POPULATION.—An accurate knowledge of the number of the population forms the basis of all vital statistics. For example, a comparison of the numbers of births in any given community with those in any other community has no significance unless the number living in each [illegible] of which these births occurred is also known.

The enumeration of the numbers of the people living in any [illegible] country is obtained from the census or [illegible] more or less frequent periods usually of ten years [illegible] In modern times the first census was taken in Sweden in 1749. The first census of the United States was taken in 1790, the last in England in 1901. For [illegible] purposes, being [illegible] in any country with sufficient [illegible] as to age and sex to satisfy the requirements of statistics and [illegible] to its inhabitants [illegible] of the numerical strength of the nation.

In the United States the census is taken periodically during the months of May to June [illegible] It is especially desirable [illegible] where the population is subject to [illegible] in consequence of the variable factor of migration that census enumerations should be made [illegible] than once in ten years. Hence a few States (Massachusetts, Rhode Island, and Michigan) take an intermediate census, which gives the advantage of a new starting-point from which to make estimates of population in intercensal years.

Various methods are adopted for estimating the population in intercensal years:

1. In a community where a strict record of emigration and immigration is kept, and a complete system of registration of births and deaths is also enforced, the population may be accurately calculated by balancing the difference between the births and deaths and the increase or decrease due to migration. This is done in the city of Berlin and in New Zealand, but is impracticable in most countries on account of the deficiency in the necessary [illegible]

2. Other methods occasionally adopted consist of estimates based upon the number of assessed polls in a city, the number of names in a city directory, the number of children of certain ages enrolled in the schools, or the number of new inhabited houses. None of these, however, can be deemed to be reliable.

3. We may assume that the annual increase during the present decade will be one-tenth of the total increase in the last decade. By this method a city of 50,000 inhabitants in 1890, increasing to 60,000 in 1900, should have 65,000 in 1905 and 70,000 in 1910. By this method, however (that of arithmetical progression), no allowance is made for the fact that the increase increases. There is a steadily increasing number of persons each year who attain marriageable ages and become parents.

4. The method now generally adopted in most countries is that which is advised and employed by the registrar-general of England, which assumes that the same rate of increase will continue as that which prevailed in the preceding period, *i.e.*, that the population increases in geometrical progression.

The following example illustrates this principle: If the census population of a city was 50,000 in 1890 and had increased to 60,000 in 1900, what is its estimated population in 1905?

Find the rate of increase from 1890 to 1900.

[illegible]

In the foregoing formula r may be taken as the ratio of increase, R being equivalent to $1 + r$.

By the same method the same city should have an estimated population of 72,000 in 1910, instead of 70,000 which would result from the application of the arithmetical method.

None of the foregoing methods can be depended upon to give accurate results in all cases, since irregularities affecting the different factors which control the population are always likely to occur. In one decade a town may experience a rapid growth in consequence of immigration, prosperous times, and a high birth rate, while in the next decade one or all of these factors may be decidedly changed. A quinquennial census is very desirable, especially in American States, where migration is an important though very variable factor.

Massachusetts, Rhode Island, and Michigan.—Unfortunately, in by far the majority of the States of the Union no complete system of registration exists, and consequently no accurate knowledge of the vital statistics of such States can be had until state legislation shall [illegible] so far advanced as to make registration compulsory.

A law was enacted in the Massachusetts colony in 1639 requiring registration of marriages, births, and deaths; but it was not until more than two centuries

[illegible]

[illegible]

[illegible]

1840 having been seriously depleted by the migration of persons of young and producing ages, so that the ratio of women aged fifteen to forty five was considerably below the average. The years to which these figures apply are the five years 1883–87, the approximate mean population of the period being that of the census of 1885. The mean annual births for the five years (1883–87) constitute the other factor.

On the other hand, if a population with an unusually high birth rate be considered, like that of Holyoke, other conditions are found to prevail. In Holyoke, during the same five years (1883–87), the mean annual birth rate was 43.3 per thousand, or twice that of Bradford and nearly thrice that of Nantucket, while the birth rate per thousand women of child-bearing ages (147.7 per thousand) was also twice that of those towns during the same period. In this instance the high birth rate was undoubtedly due to the existence among the population of a large number of French Canadians of young and producing ages, whose fecundity is proverbial.*

The birth rate in most civilized countries in the past half-century has shown a gradual tendency to decline (see table on page 263). This diminution appears to have been caused in most countries by postponement of marriage to more mature years and by a larger proportion of celibacy. In France this diminution has become so serious as to reduce the birth rate in a few recent years to a lower point than the death rate, and to awaken apprehensions as to the future stability of the population.

The chief cause of the diminution of the birth rate, according to Newsholme, is "the deliberate and voluntary avoidance of child-bearing on the part of a steadily increasing number of married persons."

Stillbirths.—The term births as heretofore used implies living births. Stillbirths, in conformity to general usage, are considered in a separate category, since, as births, they add nothing to the living population, never having lived in the sense of having a separate existence. For similar reasons, as deaths they subtract nothing from the living population and are not included in the death rate.

The deaths of still-born males are usually from 25 to 50 per cent. greater in number than those of females. In the forty years 1856–95 there were registered in Massachusetts 31,656 male still-born children and 21,202 females of the same class. These all together constituted 2.96 per cent. of all births living and dead in the same period.

Sex of Living Births.—The ratio of males to females among all births, living and dead, varies in different countries within quite narrow limits, and is usually from 104 to 107 males to each 100 females.

The following figures show the relation of the sexes at birth in different countries for a ten-year period (1871–80):

BIRTHS OF MALES TO 1,000 FEMALES.

German Empire*	1,062	Holland	1,063
Switzerland	1,063	England†	1,038
Austria	1,067	Denmark	1,058
Italy	1,071	Sweden	1,060
France	1,063	Norway	1,061
Belgium	1,058	Massachusetts‡	1,066

* The figures for the German Empire are for the years 1872–80.
† Stillbirths not included in the figures for England, which probably accounts for its difference from the other figures.
‡ The statistics for Massachusetts are for the forty years 1856–95.

The foregoing figures are the average results of over 50,000,000 births which occurred in the countries named. This difference in the number of each sex at birth partially disappears in the first years of life in consequence of the higher mortality of boys.

Plural Births.—Plural births occur with considerable regularity, those of twins constituting from a little less to a little more than one per cent. of all births, while triplets constitute a little more than one-one hundredth of one per cent. of all births. The following observations of births in several countries show slight differences in these ratios; they are the result of observations upon over twenty million births in the countries named:

RATIO OF PLURAL BIRTHS.

	Twins in 1,000 labors.	Triplets in 1,000 labors.
Switzerland*	12.2	0.12
Prussia*	12.2	.13
Bavaria*	12.4	.15
Austria*	11.7	.15
Italy*	12.1	.15
France*	9.8	.11
Sweden*	14.4	.17
Massachusetts, 1856–95	9.2	.13

* "Die Bewegung der Bevölkerung," Bern, 1885.

Illegitimacy.—In all countries where registration exists a certain proportion of the births are found to be illegitimate.

So far as the States of the Union are concerned, there is no very definite information to be had upon this point.

From such sources as are obtainable it does not appear probable that the percentage of illegitimacy in the United States is as great as that of other countries. The statistics of the large cities, and especially of those which contain foundling asylums and lying-in hospitals, show larger percentages than the rural districts.

The following table presents the illegitimate birth rates deduced from over thirty million births in the countries named:

ILLEGITIMACY IN DIFFERENT COUNTRIES.*

	Illegitimate births per 1,000 births.		Illegitimate births per 1,000 births.
The German Empire	88	England	48
Austria	140	Denmark	102
Italy	73	Sweden	101
France	54	Norway	85
Belgium	75	Switzerland	50
Holland	32	Massachusetts (1856–91)	13

* "Die Bewegung der Bevölkerung in der Schweiz," Bern.

DEATHS.—Death rates are calculated in proportion to every thousand of the living population, the unit of time being a year. This unit is employed when death rates for shorter periods (a week or month) are stated. They represent the number who would die out of each thousand of the population if the same death rate were to continue throughout the year.

The following is the best plan for obtaining the weekly death rate with accuracy:

The correct number of weeks in a year being 52.18,* if the population of a city is 250,000 and the number of deaths in a given week is 95, then the death rate for that week is 19.8:

$$\frac{250{,}000}{52.18} = 4{,}791. \qquad \frac{1{,}000}{4{,}791} = 0.2087:$$

0.2087 is the factor by which the deaths for each week, in the case of city of 250,000 inhabitants, must be multiplied.

Therefore, $95 \times 0.2087 = 19.826$ or 19.8. This is the crude death rate.

Various corrections are required to insure accuracy, the most important factors being the deaths in public institutions, visitors, and the influence of age and sex, all of which vary in different communities. The inmates of

* The birth rate of some of the lower counties of Eastern Canada in recent years has been as high as fifty-eight to sixty per one-thousand inhabitants.

* More accurately 52.17747, leap years being reckoned; but 52.18 is sufficiently accurate for practical purposes.

a public institution, hospital, asylum, sanitarium, prison, or state almshouse in a given city, town, or district may consist almost wholly of persons belonging to other districts. All deaths of outsiders occurring in such institutions should, therefore, be subtracted, and all deaths of inhabitants occurring in outside institutions should be added in estimating the death rate. The living population, so far as it is derived from outside sources, should also be excluded, as well as the deaths of such persons, in making up an estimate of death rates, in order to make the death rate approximately correct. In many of the Rocky Mountain health resorts, as well as others of the South and West, it is also customary to exclude the deaths of visitors in making up the death rate.

The Relation of the Death Rate to the Birth Rate.—While a high birth rate in a single year may be contributory to a high death rate in the same year and year following, it does not follow that a continuously high birth rate will be productive of a correspondingly high death rate. It is true that the death rate of children under five is very much higher than that of the general population, but if a high birth rate continues for several years it then increases the ratio of the total population at ages when the mortality is at its lowest point, and thus lowers the general death rate.

The Effect of Age and Sex Distribution upon the Death Rate.—Two cities, towns, or districts which are entirely alike in their climate, density of population, and sanitary conditions may have very different death rates, on account of differences in the age and sex constitution of their populations.

The population under five years of age may have a death rate of 60 per 1,000, and that of persons over sixty-five years of age may be as high as 80 or 90 per 1,000, while that of adults from twenty to sixty years of age may be only 12 per 1,000. It is therefore plain that a predominance of children under five years of age, or of persons over sixty-five, will raise the general death rate, while an excess of persons between twenty and sixty will lower it.

MASSACHUSETTS—DEATHS TO 1,000 LIVING AT EACH OF TEN GROUPS OF AGES, 1899-1901.

	All ages.	0 to 5.	5 to 10.	10 to 15.	15 to 20.	20 to 25.	25 to 35.	35 to 45.	45 to 55.	55 to 65.	All over 65.
Males	18.3	58.4	4.7	2.8	4.7	6.7	8.0	10.5	16.5	31.7	88.6
Females	16.7	48.0	4.6	2.9	4.4	5.9	7.3	9.4	14.2	26.5	82.8

ENGLAND 1881-90.

	All ages.	0 to 5.	5 to 10.	10 to 15.	15 to 20.	20 to 25.	25 to 35.	35 to 45.	45 to 55.	55 to 65.	65 to 75.	All over 75.
Males	20.3	61.6	5.4	3.0	4.3	5.7	7.8	12.4	19.4	34.7	70.4	162.7
Females	18.1	51.9	5.3	3.1	4.4	5.5	7.4	10.6	15.1	28.4	60.4	148.0

Again, an excess of males will tend to raise the death rate, while an excess of females lowers it, since, as shown in the accompanying tables, the death rate of females at all ages except from ten to twenty years is less than that of males. While it is proper, therefore, to compare the death rate of a given city for any year with that of a previous year, provided there were no material changes in the population in the intervening years, it is not safe to compare the general or crude death rates of one city with those of another without taking account of the differences in the ages and sex constitution of the populations of such cities. It is for this reason that the death rates of the older cities of the Atlantic coast cannot safely be compared with those of newly settled Western districts, where young adults between the ages of fifteen and forty-five are in excess of numbers.

In the following table the age and sex constitution of two cities are compared with that of the State at large, as an illustration of these differences. In the State at large the sexes in 1900 were in the ratio of 48.75 per cent. of males to 51.25 females, or 1,051 females to 1,000 males, while that of Boston was in the proportion of 1,040 females to 1,000 males, and that of Salem 1,109 females to 1,000 males.

CENSUS OF 1900. AGE DISTRIBUTION.

Ages.	Massachusetts		Boston.		Salem.	
	Males.	Females.	Males.	Females.	Males.	Females.
Under 5 years	505	501	510	512	530	520
5 to 10 years	457	456	437	435	506	473
10 to 15 years	407	411	378	377	411	427
15 to 20 years	411	437	356	397	405	449
20 to 25 years	461	534	467	565	449	519
25 to 35 years	921	995	1,076	1,074	842	920
35 to 45 years	704	708	780	744	631	710
45 to 55 years	470	492	462	478	448	523
55 to 65 years	292	334	253	289	286	377
All over 65 years	224	286	148	213	220	328
Unknown	25	11	35	14	13	13
	4,875	5,125	4,902	5,098	4,741	5,259
	10,000		10,000		10,000	

In Newton there were 1,234 females to 1,000 males, but in Gloucester the males predominated, there being only 873 females to 1,000 males in that city. These differences are determined largely by the character of the industries conducted in the different cities.

With reference to ages, there were in Massachusetts in 1900 52.45 per cent. of the population between twenty and fifty-five years of age, in Boston 56.46 at the same ages, but in Salem only 50.42 per cent.

Again, there were in Massachusetts 11.36 per cent. of persons over fifty-five years of age, in Boston 9.03 per cent., and in Salem 12.11 per cent.

In Boston the children under fifteen constituted 26.49 per cent. of the population, but in Holyoke those of the same age were 33.12 per cent. of the population.

All these differences have an effect upon the death rate according to the preponderance of persons at healthy ages.

Method of Correction for Age and Sex Distribution.—The method shown in the following table has been adopted by the registrar-general of England, and has been indorsed by other statisticians, notably by Körösi, whose method requires less calculation since he advises only four age periods for correction instead of eleven, as in the English tables. The periods recommended by Körösi are as follows: All under one year; all from one to twenty years; all from twenty to fifty years; all over fifty years. He also advises that the population of Sweden be taken as a standard of distribution, Sweden being a very healthy population. Dr. Ogle suggests the adoption of a combined standard, made from the seven principal European nations. The English tables employ the population of England and Wales as a standard, and in the following table (on page 250) the writer has referred each of the cities to the population of Massachusetts as a standard of comparison.

In the following table the *standard death rate* signifies the death rate at all ages, calculated on the hypothesis that the rates at each of the ten-age periods in each city were the same as those of the States during the three years, 1899–1901. The death rate at all ages in the State during that period having been 17.48 per 1,000.

The *factor for correction* is the figure by which the crude or recorded death rate should be multiplied, in order to correct for variations of sex and age distribution.

The *corrected death rate* is the recorded death rate multiplied by the factor for correction.

The *comparative mortality figure* represents the corrected death rate in each city, as compared with the recorded death rate in the State in 1900 taken as 1,000.

RECORDED AND CORRECTED DEATH RATES PER 1,000 PERSONS LIVING IN MASSACHUSETTS CITIES OF MORE THAN 25,000 INHABITANTS IN 1900.

Cities in the order of their corrected death rates.	Standard death rate.	Factor for correction for sex and age distribution.	Recorded death rate (1900).	Corrected death rate (1900).	Comparative mortality figure.
	1.	2.	3.	4.	5.
MASSACHUSETTS	17.48	1.000	18.23	18.23	1.000
Brockton	16.27	1.074	13.85	14.87	816
Malden	17.02	1.027	14.53	14.92	818
Newton	17.06	1.024	15.01	15.37	843
Haverhill	17.67	989	15.55	15.38	844
Somerville	17.30	1.010	15.67	15.83	868
Fitchburg	17.02	1.027	15.67	16.09	883
Chelsea*	17.77	984	16.42	16.16	886
Lynn	16.80	1.040	15.91	16.55	908
Gloucester	17.33	1.009	17.00	17.15	941
Cambridge	16.54	1.056	16.54	17.47	958
Springfield	17.31	1.010	18.93	19.12	1.049
Salem	17.95	974	19.86	19.34	1.061
Worcester*	16.56	1.056	18.33	19.36	1.062
Taunton*	16.89	1.035	19.43	20.09	1.103
Lowell	16.07	1.088	19.48	21.19	1.162
Boston*	16.26	1.075	20.08	21.59	1.184
New Bedford	17.07	1.024	21.19	21.70	1.190
Lawrence	16.09	1.086	20.40	22.15	1.215
Fall River	15.90	1.099	21.53	23.66	1.297
Holyoke	15.55	1.124	21.96	24.68	1.354

* Correction has been made in the four cities of Worcester, Taunton, Chelsea and Boston for deaths of non-residents occurring in sixteen public and private institutions, 119 deaths in Worcester, 73 in Taunton, 90 in Chelsea, and 419 in Boston.

The figures in the last column may be read as follows: After making approximate correction for differences of age and sex distribution, the same number of living persons that gave 1,000 deaths in Massachusetts in 1900 gave 816 in Brockton, 1,184 in Boston, 1,354 in Holyoke, etc.

The first column in the table is obtained by assuming that the mean mortality in Massachusetts in 1899–1901 prevailed in each of the twenty cities in the list.

The age and sex distribution of each city at the last census (1900) being known, the mean mortality in Massachusetts (1899–1901) is applied to the population thus constituted, producing as a result the series of death rates in column 1. The differences between the cities in this column are consequently caused only by the difference in age and sex distribution. As an example of the method of obtaining these *standard death rates*, the figures for Boston may be taken (see the following table). Here the total population of Boston in 1900 was 560,892. The whole number of calculated deaths was 9,122. The standard death rate for that year was therefore $\frac{9{,}122 \times 1{,}000}{560{,}892} = 16.26$ per 1,000, as shown in the foregoing table.

Now the mean annual death rate of Massachusetts for the three years 1899–1901 was 17.48. This ought to be the same as the calculated death rate for Boston, which was obtained by applying the mean annual death rate of the State at the different age groups to the population of Boston at these age groups.

But this standard death rate of Boston was lower, as shown in the table, which arises from the fact that the distribution of age and sex in the Boston population is more favorable than that of the State at large (see table, page 249).

The standard death rate being lower for Boston, must be raised in order to bring it into comparison with the death rate of the State; that is, it must be increased in the proportion of 16.26 to 17.48. This fraction $\frac{17.48}{16.26} = 1.075$. This number 1.075 is the factor for correction for age and sex distribution by which the crude or recorded death rate of Boston must be multiplied in order that it may be comparable with that of the State.

By multiplying the recorded death rates in column 3 by the factors for correction, the corrected death rates are obtained as given in column 4. These are the death rates which would have been recorded in each city had its population been identical, so far as age and sex distribution are concerned, with that of the State.

Ages.	Mean Annual Death Rate in Massachusetts, 1899-1901, per 1,000 Living at Each Group of Ages.		Population of Boston in 1900.		Calculated Deaths in Boston (1900).	
	Males.	Females.	Males.	Females.	Males.	Females.
0–5 years	58.41	48.00	28,628	28,733	1,672	1,379
5–10 "	4.74	4.60	24,495	24,401	116	112
10–15 "	2.84	2.88	21,202	21,160	60	61
15–20 "	4.70	4.43	19,965	22,289	94	99
20–25 "	6.71	5.94	26,199	31,661	176	188
25–35 "	7.96	7.31	60,362	60,242	481	440
35–45 "	10.48	9.42	43,748	41,717	458	393
45–55 "	16.26	14.20	25,910	26,816	421	381
55–65 "	30.96	26.51	14,145	16,231	438	430
65 and over	88.60	82.78	8,301	11,919	735	987
Unknown	.....	.....	1,967	801		
			274,922	285,970	4,652	4,470
			560,892		9,122	

This principle in vital statistics is specially applicable to those towns from which, in consequence partly of local conditions, the young and vigorous portion of the population has emigrated, as in the case of Nantucket, Mass., which in 1840 had a population of 9,012; but this number had diminished to 3,142 in 1885. Of this population of 3,142, only 43.8 per cent. were between the ages of twenty and fifty-five, when the death rate is low, as compared with 52.4 per cent. at the same ages in the State at large. The percentage of the population who were over fifty-five (at which ages the death rate is high) was 29.6, as compared with only 11.4 in the State at large in the same census year. As a consequence, Nantucket in that year should be credited with a standard death rate of 27.02, a factor for age and sex correction of 0.733. The crude or recorded death rate of the town was 33.74 per thousand, the corrected death rate 24.73, and the comparative mortality figure 1,261.

According to F. L. Hoffmann, the fallacy of disregarding the effect of age distribution is shown in a recent United States Government report, wherein it is stated that "the significance of the annual *rate of death* from disease in the Philippines (17.2 per thousand) may be better appreciated by comparison with the rates in some of our well-known American cities. Mr. Root gives a table showing the annual death rates of Washington, Boston, etc., together with the mortality rate from disease of soldiers in the Philippines. Even a moment's reflection would have made it clear that a comparison of the death rate of soldiers, mostly of ages from eighteen to thirty, could not properly be made with the mortality of the general population at all ages. Even a comparison with the general death rate of cities, at ages from fifteen to forty-five, which, according to the then available census of 1890, was 10.9 per thousand, would not have been accurate, in that soldiers represent a carefully selected class of physical risks in contrast to the general population, which includes the sick and otherwise physically impaired. The only accurate method of comparison which could have been suggested to the Secretary of War by the surgeon-general of the army would have been the average mortality rate from disease of soldiers in the United States army previous to the war with Spain.

But by this method the argument advanced by Mr. Root could not have been proven, for, according to the annual reports of the surgeon-general, the mortality of soldiers from disease during the five years, 1891–95, was at the rate of 4.3 per thousand, while during 1896 the rate was 3.8, and during 1897 it was 3.1. In other words, the mortality of soldiers in the Philippines from disease was four times as great as the mortality from disease of United States soldiers under conditions of peace." (F. L. Hoffmann, in Transactions of American Statistical Association, December, 1902, p. 198.)

INFANT MORTALITY.—The mortality of infants under one year of age should not be compared with the general population, since the relative number of living infants varies much in different communities. A more correct method is to compare the deaths of infants one year old with the living infants of the same age. It has not been found practicable, however, by ordinary census methods to find the number of infants with accuracy. This is shown by the census figures of almost any State or country for the first five years of life.

For example, the figures for Massachusetts in the state census of 1885 and the United States census of 1900 were as follows:

NUMBER OF CHILDREN LIVING AT CERTAIN AGES

Years.	State Census 1885.	U. S. Census (1900).
0–1 year	55,888	60,492
1–2 years	47,325	53,943
2–3 "	40,555	50,256
3–4 "	38,061	46,678
4–5 "	36,706	44,865

In the foregoing table the numbers of children found who were under two years of age, but over one year, were less in each census than those who were a year older as well as less than those who were a year younger. But since immigration does not largely affect the numbers at these early ages, we should naturally expect to find a diminishing series beginning with the first year of life, the deaths making the numbers for each successive year of life less and less. This error appears in the eighth census also, and in order to obtain the number of infants under one year correctly it is necessary to calculate a redistribution of these early years, or, what is preferable, to use the births as a standard.

For the purpose of greater accuracy, the deaths under one year occurring in a calendar year should be compared with the births of an earlier period, since many of the infants under one year dying in any year were born in the previous year. For this reason it is customary to employ as a standard of comparison the births occurring in a year ending with June 30th, and to compare with this number the deaths under one year occurring in the calendar year ending December 31st.

Upon this basis, the infant mortality of Massachusetts during the twenty years, 1856–75, was 150.3 per thousand births, and that of the succeeding twenty years, 1876–95, was 161.2 per thousand, the mean of the forty-year period being 156.7. The births employed in this calculation were those which occurred during the period beginning July 1st, 1855, and ending June 30th, 1895; and the deaths under one year were those which occurred in the forty calendar years, 1856–95, inclusive.

The infant mortality of the five following years, 1896–1900, was respectively 167.7, 148.1, 149.1, 148.0, and 159. The infant mortality of cities is usually greater than that of the rural districts. In Massachusetts, in the ten years 1881–90, the infant mortality of the cities was 174.9 per thousand births, and that of the rural districts was 129.5. The following table presents the infant mortality of several countries:

INFANT MORTALITY.* DEATHS UNDER ONE YEAR TO 1,000 BIRTHS.

Countries.	Years.	Infant Mortality per 1,000 Births.	Countries.	Years.	Infant Mortality per 1,000 Births.
Ireland	1884–88	94	Italy	1884–91	192
Sweden	1881–90	97	Prussia	1886–92	206
Scotland	1885–90	120	Hungary	1884–87	212
England	1885–91	144	Austria	1886–87	246
Belgium	1881–91	159	Saxony	1883–92	281
France	1885–90	165	Bavaria	1879–88	287
Holland	1885–90	179			

* From paper by Dr. Eross, in Koch's Zeitschrift f. Hygiene, vol. 19, 1896, p. 371.

An important factor in relation to infant mortality is the method of feeding. The best information upon this point comes from the city of Berlin, where, for several years, all infants have been classified with reference to the method of feeding, so that the ratio of deaths of each class could be estimated.

The results of these observations extending over a series of years were as follows. Mortality per thousand infants under one year old in Berlin:* Among those who were fed on the mother's milk only, 7.4 per 1,000; on mother's milk and cow's milk, 21.4 per 1,000; on cow's milk alone, 42.1 per 1,000; on milk substitutes, 67.7 per 1,000; on cow's milk and milk substitutes, 125.7 per 1,000. These figures are the result of observations upon 65,720 deaths of infants under one year old in Berlin.

The health commissioner of Buffalo claims a large reduction in the infant mortality of that city by the suppression of the sale of nursing-bottles having long tubes attached and by other ordinances of a similar character.

Effect of Intemperance and Poverty upon Infant Mortality.—It is hardly necessary to assert the effect of these factors in the causation of infant mortality. In every country the records show their damaging effects. Cities in which intoxicating liquors are freely sold under license laws have a higher infant mortality than those cities in which such sale is forbidden by the popular vote. In the census year 1895, the infant mortality in the seventeen cities of Massachusetts in which licenses were granted was 174 per 1,000 births, while in the cities in which no licenses were permitted the infant mortality was only 122 per 1,000. In this estimate no account was taken of those few cities in which the sentiment of the voting population was so equally balanced that a change from license to no license, or *vice versa*, took place during the year in question.

The effect of poverty is shown in Dr. Billings' census volume relating to the vital statistics of certain cities, wherein the mortality of children under five years of age in one ward of a certain city inhabited by a poor class of residents was 157.1 per 1,000 living of the same age, while a neighboring wealthy district had a mortality of only 40.4 for the same class.

Again, the average pay of shoemakers is from sixty to ninety per cent. greater than that of cotton and woollen operatives. The infant mortality of the three shoe-manufacturing cities of Lynn, Haverhill, and Brockton for the ten years 1881–90 was 146.1, while that of the cotton factory cities Fall River, Lowell, and Lawrence for the same period was 227 per 1,000 births.

Effect of High Birth Rate.—That a high birth rate is not necessarily a concomitant of high infant mortality is shown by Dr. H. May in a letter to *Public Health* (March, 1903), in which he shows that while the birth rate had fallen in each of the following large cities, the infantile mortality had risen.

* International Statistical Bulletin, vol. ii., No. 2, p. 14.

City.	Birth Rate.		Fall in birth rate. Per cent.	Infantile Mortality.	
	1876.	1901.		1876.	1901.
Salford	49.3	29.2	43.0	189	204
Manchester	39.8	29.1	27.0	180	199
Birmingham	42.8	32.1	25.0	160	187
England and Wales	36.3	28.5	20.5	146	151

Density of population has an influence upon the death rate. The death rate of rural districts is lower than that of cities, as a general rule. The urban districts of England in 1899 had a death rate of 19.2 per 1,000, while that of the rural population was only 16.3. In Massachusetts the death rates in 1890 and 1900 in the urban and rural populations were respectively 20 and 18.5 per 1,000 in the urban districts and 17.8 and 17.3 in the rural districts. It is only when the density has reached a certain degree of intensity that it begins to assert an appreciable effect. Even then it is what is implied in or is an attendant upon aggregation, rather than the aggregation itself, that is harmful. Poverty and intemperance are usually greater in densely populated districts than elsewhere, with their accompaniments of deficient food and clothing and bad housing. Hence the excess of phthisis in tenement-houses, and especially in those tenements consisting of two or three rooms only. Newsholme says that "the true density that should be considered is the number of persons to each room, not the number of persons on a given area" ("The Vital Statistics of the Peabody Buildings," Royal Statistical Society, February, 1891).

Dr. Farr had proposed an extremely mathematical rule or formula for the calculation of the death rates of populations of different density, stating at first that the mortality increases in proportion, not to the density of population, but to the sixth root of the density. This formula he afterward changed to the eighth root approximately, or, more exactly, to 0.11998.

By this formula if d and d' = density of population of two places, and m and m_1 = mortality of population,

$$\text{then } \frac{m}{m} = \sqrt[8]{\frac{d'}{d}} \text{ and}$$

$$m : m :: \sqrt[8]{d} : \sqrt[8]{d}$$

In 345 English districts which had a mortality of 19.2 per 1,000, the density was 186 persons per square mile. What was the mortality in 9 of these districts which had a high density of 4,499 per square mile?

$$\frac{m}{19.2} = \sqrt[8]{\frac{4499}{186}} \qquad m = 28.6$$

So closely was the ratio found to be followed in places whose sanitary conditions were fairly the same, and which differed only in density of population, that Dr. Farr proposed that in any sanitary inquiry the influence of density should first be discovered by means of the foregoing formula, and that the effect of other influences above or below this should then be investigated. But the death rate has declined in recent years, as density has increased. In England the density of population has increased from 307 per square mile in 1851 to 497 in 1891, while the death rate meanwhile has declined from 22.5 to 19.1 per 1,000 in the same time. In New England the density increased from 75.8 in 1890 to 90.2 per square mile in 1900, while the death rate decreased as follows: In 1892, 19.9; in 1893–97, 18.3; in 1898–1900, 17.3.

With Newsholme, therefore, we are led to believe "that either the relationship between density of population and mortality is accidental rather than essential, or that countervailing influences are at work."

While, therefore, this strict mathematical formula may be applicable to the densely crowded portions of large cities when compared with each other, it does not necessarily apply when the condition of one district is compared with its own condition at an earlier period when the density was much less. Nor can it be employed in comparing the populations of cities and districts in the United States, without careful correction for age and sex distribution.

In the three States of Maine, New Hampshire, and Vermont, with an average density of population of 30.2 per square mile, the death rate in the nine years 1892–1900 was 16.90; but in the three States, Massachusetts, Rhode Island, and Connecticut, with an average density of 296.5 per square mile, the death rate in the same period was 18.55 per 1,000.

To a certain degree the number of rooms occupied by a given number of people bears a definite relation to the density of population as well as to its social condition, and hence has a direct effect upon the death rate, as shown in the following table for the city of Glasgow:*

Size of houses.	Census population (1901).	Deaths from all Causes.		Infectious Diseases.		Phthisis.		Respiratory Diseases including Croup.	
		Deaths.	Death rate.	Deaths.	Death rate.	Deaths.	Death rate.	Deaths.	Death rate.
One room	104,128	3,405	32.7	771	7.4	247	2.4	792	7.6
Two rooms	348,731	7,418	21.3	1,576	4.5	620	1.8	1,600	4.6
Three rooms	151,754	2,081	13.7	290	1.9	178	1.2	362	2.4
Four rooms and more	136,511	1,533	11.2	139	1.0	99	.7	272	2.0
Whole city			20.6		3.8		1.8		4.3

The Effect of Occupation upon Mortality.—The occupation or calling in which persons are engaged has an influence upon the health and consequent length of life of those who are thus employed, some occupations being more favorable to health than others.

Various methods have been adopted for measuring the comparative healthfulness of occupations. For several years it was customary in some of the older States to give the *mean age at death* of persons engaged in different occupations and thus to compare them with each other. This method, however, is entirely fallacious. For example, the average age at death of judges in Massachusetts was 65.9 years, of clerks 36.4 years, and of students 23.7 years. These figures obviously have no value as determining the comparative length of life or healthfulness of the persons engaged in these employments.

Nor is it a strictly correct method to compare the number dying in any given occupation with the number engaged in such occupation, since the persons entering upon the duties of one occupation may do so at a much earlier or later age than those entering another occupation which may be compared with it.

According to Newsholme,† the only trustworthy method is to compare the mortality of those engaged in one occupation and of a given age, with the mortality of those engaged in another occupation and of a corresponding age.

The circumstances which render certain occupations injurious to the health of persons engaged in them are overcrowding and defective ventilation, extremes of

* "The Death Rate in One-Apartment Houses," by A. K. Chalmers, M.D., Medical Officer of Health of Glasgow, 1903.

† "Vital Statistics," third edition, page 172.

heat and cold, inhalation of noxious vapors, and especially of dust, both organic and inorganic, exposure to lead and other poisons, mental anxiety, and exposure to intemperance.

Observations upon the mortality of occupations in American communities are generally untrustworthy and inaccurate; first, because of wrong methods adopted; and second, because of the shifting and unstable character of persons employed, as compared with those engaged in foreign industries.

The following table, constructed by Dr. Tatham from the registrar-general's returns of England for the years 1890–92, may be deemed accurate for English occupations. It embraces the statistics of death of 61,215 men who were engaged in the occupations named in the table.

Occupations.	Ages. 25–35 years	35–45 years	45–55 years	55–65 years	Comparative mortality figures.
Clergyman, priest	4.86	4.23	5.18	10.52	533
Lawyer, solicitor	5.32	10.67	17.72	34.50	821
Physician, surgeon	6.69	14.92	21.04	34.16	936
Commercial traveller	6.09	12.62	21.41	39.28	961
Farmer, grazier	4.29	7.03	11.20	23.97	563
Agricultural laborer	5.54	9.14	13.56	24.83	666
Fisherman	9.13	10.60	18.61	25.65	845
Innkeeper, bartender, etc.	15.21	23.32	34.84	53.18	1,642
Innkeeper's servant	15.06	24.52	35.24	52.68	1,659
Grocer	5.40	8.62	14.34	24.92	664
General shopkeeper	8.89	14.03	19.92	32.59	953
Printer	9.10	14.40	21.56	43.39	1,096
Butcher	7.53	15.66	22.65	43.32	1,096
Corn miller	5.07	9.33	18.90	38.88	845
Hatter	6.96	15.35	24.57	43.90	1,109
Baker, confectioner	6.49	11.00	22.18	35.45	920
Tailor	6.86	13.67	21.98	37.59	989
Hairdresser	9.41	15.01	23.28	39.03	1,099
Shoemaker	7.66	11.35	19.85	35.25	920
Tanner	5.78	6.40	18.69	32.78	756
Currier	6.79	12.65	22.16	40.62	998
Tool, scissors, file, saw, needle maker	8.36	18.38	32.93	57.52	1,412
Blacksmith	5.80	10.81	20.74	39.45	914
Copper, lead, tin, zinc worker	7.45	13.98	24.55	46.02	1,123
Bricklayer, mason	6.55	13.45	22.04	40.23	1,001
Carpenter, joiner	5.78	9.36	15.19	32.15	783
Plumber, painter, glazier	7.04	14.79	25.13	45.58	1,120
Woollen operatives	6.99	11.99	20.58	45.75	986
Cotton, flax, linen operatives	7.13	13.58	25.11	55.06	1,176
Wool, silk, cotton dyer and printer	10.90	16.14	28.05	57.95	1,370
Potter, earthenware maker	8.19	19.58	42.97	75.13	1,706
Coal miner	6.29	9.63	19.42	43.79	935
Tin miner	8.06	14.32	33.20	66.09	1,409
Glass maker	11.32	17.88	32.14	60.79	904

In the foregoing table, the first four columns of figures present the death rates at four different ages of persons engaged in the specified occupations. For example, the death rate of clergymen, twenty-five to thirty-five years of age, is 4.86 per 1,000; of innkeepers of the same age, 15.21 per 1,000. The figures in the last column should be read as follows: The same number of men (aged twenty-five to sixty-five years) that would give 1,000 deaths among all males (as a standard of comparison) would give 533 among the clergy, 563 among farmers, 1,642 among innkeepers and bartenders, 1,412 among steel grinders, etc.

When the mortality of persons in different occupations is distributed according to the causes of death, we find more specific results of the effect of such industries on the health of the employed. The highest mortality from cancer among occupied males is found among chimney-sweeps. For phthisis the lowest mortality is found among clergymen, railway engineers and stokers, farmers and coal miners; and the highest among steel grinders, lead miners, costermongers, and hotel servants. Pneumonia causes a low mortality among teachers and the clergy, and a high mortality among hotel servants, dock laborers, iron workers, and coal heavers. Diseases of the liver cause low mortality among the clergy and railway porters, and high mortality among lawyers, brewers, physicians, and publicans.

The following table* is interesting as showing the effects of dust-laden air in different occupations:

Occupation.	Phthisis and diseases of the respiratory system.	Occupation.	Phthisis and diseases of the respiratory system.
Agriculturist	100	Agriculturist	100
Iron miner	133	Quarryman	261
Carpenter	148	Zinc worker	266
Coal miner	156	Iron and steel worker	292
Corn miller	166	Gunsmith	294
Baker	177	Copper miner	307
Blacksmith	177	Copper worker	317
Wood worker	202	Lead miner	319
Tin worker	204	Glass worker	335
Carpet and rug maker	213	File maker	373
Bricklayer, mason	215	Tin miner	400
Cotton worker	244	Cutler, scissors maker	407
Lead worker	247	Potter, earthenware maker	453
Chimney-sweep	249		

This table is to be read as follows: In each 100 deaths of agriculturists out of a given number employed in such occupations, there would be 133 deaths of iron-miners employed in that occupation, etc. Dr. Ogle points out that the dust of coal and wood is least injurious, that of metals and stone most injurious, while flour dust and that of textile factories occupy an intermediate position in their effects upon health.

Lead Poisoning.—The mortality of all males from lead poisoning being taken as 1, that of printers is 3, lead miners 5, gasfitters 6, coachmakers 7, copperworkers 8, glassmakers 12, potters 17, painters and glaziers 18, plumbers 21, file-makers 75, and lead workers 211.

Alcoholism.—The returns under this head are usually imperfect, but since the intemperate use of alcoholic drinks damages most of the viscera, the excess of deaths from nervous diseases, phthisis, kidney diseases, gout, and suicide in different occupations forms an index of the effect of alcoholism upon health.

In the following table the mortality of occupied males between twenty-five and sixty-five years of age from each cause of death is taken as 100, and the mortality in each industry is reduced to a figure proportional to that standard:†

	Alcoholism and diseases of the liver.	Alcoholism.	Diseases of the liver.	Gout.	Diseases of the nervous system.	Suicide.	Phthisis.	Diseases of urinary organs.
Occupied males	100	100	100	100	100	100	100	100
Coachman, cabman	153	215	122	300	100	143	124	132
Costermonger	163	277	107	150	170	100	230	171
Coal heaver	165	223	137	....	120	50	116	122
Fishmonger	168	215	144	150	109	150	86	120
Musician	168	223	141	450	135	164	174	141
Hairdresser	175	269	130	400	109	250	149	78
Dock laborer	195	400	96	150	139	157	176	166
Chimney-sweep	200	454	78	....	100	221	141	144
Butcher	238	269	207	300	128	164	105	117
Brewer	250	315	219	500	152	121	148	190
Innkeeper's servant	420	815	230	550	132	179	257	188
Innkeeper	733	708	744	600	195	229	140	220

THE CAUSES OF DEATH.—These are usually stated either in proportion to the number of deaths from all causes or as a ratio of the living population. The latter is the preferable method.

The first plan may be adopted when it is desired to ascertain the proportional share of any given cause of death in the total mortality, but for general purposes the population should be the standard of comparison.

For a half century or more diseases have been classified in most English-speaking countries in accordance with

* Newsholme's "Vital Statistics," third edition, p. 183.
† Newsholme's "Vital Statistics," third edition, p. 184.

the plan proposed by Dr. William Farr about the middle of the last century. The principal groups of this system were termed the zymotic, constitutional, local, developmental, and violent classes of disease or causes of death. The progress of medical science, however, has demanded a change, and the Bertillon system of classification has in many countries superseded the system of Dr. Farr. According to this new system, the groups of causes of death are as follows: (1) General diseases; (2) diseases of the nervous system; (3) diseases of the circulatory system; (4) diseases of the respiratory system; (5) diseases of the digestive system; (6) diseases of the genito-urinary system; (7) childbirth; (8) diseases of the skin; (9) diseases of the locomotor system; (10) malformations; (11) early infancy; (12) old age; (13) violence; (14) ill-defined diseases.

These changes in classification do not in the least interfere with the study of separate causes of death, when it is desirable to compare their present and past incidence upon the population.

A general consideration of the principal infectious diseases shows, in nearly all nations or communities in which registration records are kept, a remarkable decrease, while the diseases of special organs, or local diseases as they have usually been termed, together with cancer, have shown a decided increase. In Massachusetts, for example, the group of diseases embracing smallpox, measles, scarlet fever, diphtheria, typhoid fever, cholera infantum, consumption, whooping-cough, dysentery, and the diseases incident to childbirth had decreased from a mean of 81.7 per 10,000 living in the five-year period 1856–60 to 50.5 per 10,000 in the five-year period 1891–95; while, on the other hand, the group embracing pneumonia, kidney diseases, heart diseases, brain diseases, and cancer had also increased from a mean of 27.7 per 10,000 in the five-year period 1856–60 to 68.8 in the period 1891–95.

Longstaff, in his "Studies of Statistics," shows that similar changes have taken place in England.

Tuberculosis.—This disease, which until a quite recent period has been for at least a half-century and probably much longer the most destructive disease of the human race, has shown a steady decline in mortality in those countries where records have been kept. In England this decrease has been from a mortality of 2,579 per million living among males in the period 1851–60 to 1,487 per million in 1901, and from 2,774 among females to 1,054 in the same time. This shows a greater fall among females than among males, and the same is true of Massachusetts, where the phthisis death rate fell among males from 3,166 per million in 1851 to 1,690 in 1902, and among females from 4,600 per million in 1851 to 1,504 in 1902. The death rate for both sexes from this cause declined still further to 1,595 per million in 1902.

Newsholme says, in treating of this remarkable decrease: "It is possible that, owing to more accurate statement of causes of death, there has been considerable transference from phthisis to diseases (other than phthisis) of the respiratory organs. The term phthisis is now not so loosely used as formerly, when any chronic chest affection received this name. But that this is by no means a complete explanation of the decrease in phthisis is evidenced by the fact that while the mortality from phthisis has decreased at all age groups, the mortality from respiratory diseases has only increased under five and over seventy-five years of age. Furthermore, the mortality from phthisis chiefly takes place between the ages of fifteen and fifty-five years, while that from respiratory diseases is very low during these years and greatest at the extremes of life."

A circular of the imperial board of health of Germany published in 1896 states that out of each thousand deaths during the wage-earning period of life (fifteen to sixty years) there were from tuberculous diseases in Vienna 459 deaths, in Paris 400, in Belgium 371, in Bavaria 359, in the German empire 322, in Denmark 297, and in England 223.

Typhoid Fever.—As an index of the sanitary condition of a community, the death rate from typhoid fever holds high rank, and especially as a proof of the purity of the public water supply. Since the general introduction of public water supplies in cities and towns, the death rate from this disease has steadily fallen.

Ages. The highest relative mortality from this disease is at the ages fifteen to thirty years in both sexes.

Seasons. Typhoid fever proves most destructive in the months of September, October, and November, the number of deaths from this cause in New England occurring after September 1st in each year being usually about as many as those which precede that date.

In those cities in which public water supplies have been introduced, the typhoid death rate has fallen from 21 per 10,000 in Munich to 6.3, in Dantzic from 9.9 to 2.4, in Berlin from 9.2 to 2.9, in Vienna from 12 to 2.1, in London from 10.2 to 4.5, and in Lawrence, Mass., from 13.4 to 1.6, the periods which elapsed varying from five to forty years. In Lawrence the death rate from this cause fell within a few weeks after the introduction of filtered water from 10.5 in 1892 to 4.8 in 1894, the filter being introduced in 1893.

The general decline in this death rate in Massachusetts is illustrated by the following diagram and table, in which the typhoid death rate is compared with the *percentage of the population not supplied with public water*, since it is among this portion of the population that typhoid fever largely occurs. Many people even in large cities still derive their water supply from polluted sources, wells, springs, and canals in manufacturing cities.

TYPHOID FEVER IN MASSACHUSETTS.

Period.	Death Rate from Typhoid Fever, per 100,000.	Percentage of Population Not Supplied with Public Water.
1856–65	92.9	75.4
1866–75	80.8	58.9
1876–85	47.4	31.7
1886–95	36.4	13.9
1901	19.5	8.5

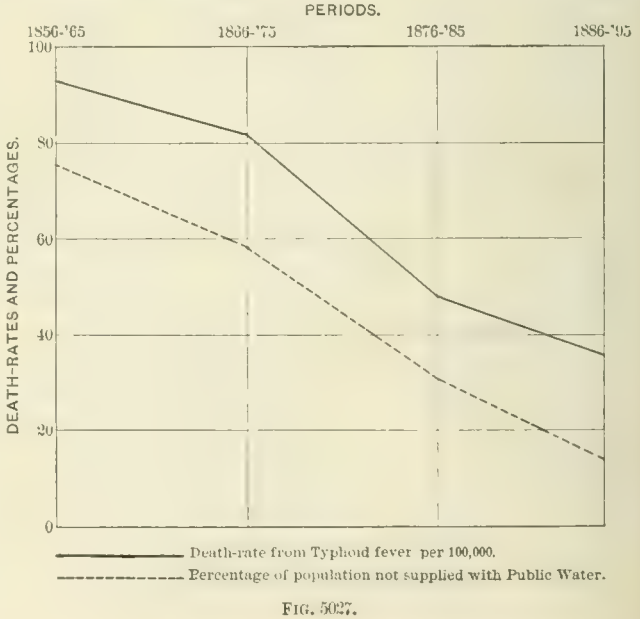

FIG. 5027.

Scarlet Fever.—This disease proves most destructive in the second, third, fourth, and fifth years of life. Three times as many die of it in the first five years of life as in the second five years, and about fifteen times as many as in the period ten to fifteen years.

The death rate of the two sexes is nearly equal, and the number dying in the first half of the year is considerably greater than those who die in the second half.

The death rate from this cause declined in England from over 9 per 10,000 in 1866–70 to 2 in 1891–95. It also declined still further to 117 per million in 1899, which was the lowest death rate in that country from this cause on record. A similar decline has been observed in many other countries, and may undoubtedly be attributed to the introduction of more efficient methods of isolation and control of infectious diseases.

Measles.—The deaths from this disease are also greatest in number in infancy and childhood, the mortality in the first five years of life being eight or ten times as great as in the second five years. The deaths of the two sexes from this cause are nearly equal. (In Massachusetts in twenty years there were 4,015 deaths of males and 3,934 of females from measles.) The deaths from this cause in the first six months are usually greater in number than those which occur in the last six months of the year. The death rate from this cause has declined in most countries, but not so decidedly as in scarlet fever.

In England it was 315 per million in 1899, or the lowest rate recorded since 1881.

In Massachusetts it was 159 per million in the twenty years 1856–75, and only 90 per million in the twenty years 1876–95.

Whooping-Cough.—This disease is more fatal in the first year of life than in any succeeding year. More females die of it than males, and the death rate from this cause has diminished, the rate in England in 1899 having been 319 per million, or the lowest yet recorded except that for 1895, which was 316. That of Massachusetts had declined from 220 per million in the twenty years 1856–75, to 140 in the twenty years 1876–95.

Diphtheria.—The figures for diphtheria are now usually considered together with those of membranous croup. The mortality is greatest in the second, third, fourth, and fifth years of life, that of the third and fourth years combined being slightly greater than those of the second and fifth years. The death rates of the sexes are nearly the same in diphtheria, but of the deaths registered as from croup those of males are slightly in excess.

The effect of seasons upon the prevalence of this disease is quite uniform and well marked, the lowest death rate usually occurring in midsummer (June to August), after which the rate rapidly rises to November, and continues at a high rate until January or February, after which the decline is more gradual than the rise in the autumn. There is reason to believe that the rapid rise in autumn as related to the opening of the schools is more than a mere coincidence.

Its prevalence from one period to another for a long series of years has been quite irregular as shown by the following figures for Massachusetts, embracing the statistics of 64,281 deaths from this cause:

Five-year periods.	Deaths from diphtheria.	Death rate per 10,000 living.	Five-year periods.	Deaths from diphtheria.	Death rate per 10,000 living.
1856–1860...	2,949	4.9	1881–1885....	8,944	9.5
1861–1865...	7,710	12.3	1886–1890....	8,857	8.4
1866–1870...	3,664	5.3	1891–1895....	7,652	6.4
1871–1875...	5,038	6.4	1896–1900....	6,331	4.7
1876–1880...	13,676	15.8			

With reference to the fatality of this disease (ratio of deaths to cases) a marked change has taken place since the general introduction of antitoxin treatment in 1894–95. Previous to its introduction the fatality of diphtheria ranged from 25 to 40 per cent. in different localities. In Massachusetts it was 28.3 per cent. for the four years 1891–94, but this percentage has been cut down to 13.1 per cent. for the seven years 1895–1901, and in 1901 it was only 10.5 per cent. The meaning of these figures, according to the Thirty-third Annual Report of the State Board of Health of Massachusetts is a saving, in the seven years, of 10,697 lives, and even if all sources of error were to cut down this figure by one-half "the result would be the saving of more than 5,000 lives by the use of antitoxin in the seven years 1895–1901."

There has also been a decided reduction in the death rate from dysentery and from puerperal fever and the diseases incident to childbirth, these latter being coincident with the introduction of antiseptic methods in the management of the lying-in chamber.

In Prussia the death rate of women in childbirth has been diminished from 81.8 per ten thousand births in the five years 1856–60 to 43.3 in the three years 1891–93, or nearly one-half. These figures are the results of observations upon over 44,000,000 cases of labor, and 296,867 deaths in childbirth.*

Smallpox.—The statistics relating to this disease and its relation to the practice of vaccination may be found fully stated in the article on *Vaccination*.

Other causes of death from which the death rate has increased. The foregoing causes of death in which the death rate has fallen during the past half-century are of the infectious class, and are mainly the diseases of children and young adults. Had the death rate from all other causes remained stationary this decided fall in that of infectious diseases would have caused a material reduction in the general death rate, an observation which applies to most countries where vital statistics are carefully recorded. But the death rate from most of the diseases, usually known as local diseases, has increased in a ratio nearly equal to the decline in infectious diseases. For example, Longstaff in his "Studies of Statistics," p. 230, presents the following table, which may be termed the balance of mortality:

ENGLAND.

The death rate from each of the following diseases per million inhabitants has fallen from the five years 1850-54 to the five years 1875–79, as follows:	
Phthisis	694
Developmental diseases	617
Fever (mostly typhoid)	569
Dropsy	405
Convulsions	342
Cholera	287
Smallpox	197
Scarlet fever	173
Tuberculous meningitis	111
Sudden death (cause unknown)	101
Diarrhœa	85
Disease of stomach and intestines	68
Measles	64
All other causes	299
	4,012

The death rate from each of the following diseases per million living has risen, 1850-54 to 1875–79, as follows:	
Lung diseases	1,213
Heart diseases	696
Brain diseases	378
Kidney diseases	229
Liver diseases	32
Cancer	191
Diphtheria	69
Tabes mesenterica	65
Whooping-cough	45
Rheumatism	45
	2,963
Balance, a fall per million of	1,049

There are several points of interest in the foregoing table:

1. Most of the destructive infectious diseases are found in the column of those in which the death rate has fallen, while the local diseases, or diseases of special organs, are found in the other column of causes in which the death rate has risen.

2. The former class, including phthisis, are chiefly diseases of children and young adults, while the latter, the local diseases and causes, are diseases of advanced life.

3. The decided fall in some instances may be taken as an evidence of more exact diagnosis of disease, as in the case of "dropsy," a symptom only which is now more commonly certified under its correct title of heart, kidney, or liver disease, hence the lessened number of cases attributed to this indefinite cause.

* Dr. H. B. Brennecke. in Vierteljahrsschrift f. öff. Gesundheitspflege, 1897, p. 81, vol. xxix.

4. The fall in the death rate from typhoid fever "is without doubt," as Longstaff states, "the great triumph of the sanitary reformers." Undoubtedly, a large share of the fall in phthisis, smallpox, scarlet fever, and measles may reasonably be attributed to the same cause.

5. The steady rise in the death rate from cancer has given occasion for comment and investigation in all countries where registration of deaths is made.

The following figures show the increase of cancer in the countries and cities named:*

Various Countries.

In Germany, while the population increased from 1880 to 1900 14.18 per cent, cancer increased in 10 states in a shorter period (1892-93 to 1898-99) 24.56 per cent.
In Ireland cancer increased with a diminishing population from 5.8 per 10,000 in 1897 to 6.5 in 1901, or in absolute numbers, 2,635 to 2,803 deaths.
In Austria from 5.4 per 10,000 in 1891 to 7.0 in 1900.
" Bavaria from 8.9 per 10,000 in 1891 to 9.9 in 1900.
" Holland from 7.9 per 10,000 in 1891 to 9.3 in 1900.
" Italy from 4.3 per 10,000 in 1891 to 5.2 in 1900.
" Norway from 6.1 per 10,000 in 1891 to 9.2 in 1900.
" England from 5.1 per 10,000 in 1880 to 8.3 in 1899.
" Switzerland from 11.4 per 10,000 in 1889 to 13.2 in 1898.
" 250 cities of France from 8.4 per 10,000 in 1887-90 to 11.0 in 1900.

New England States.

" Maine from 6.1 per 10,000 in 1891 to 7.6 in 1900.
" New Hampshire from 5.6 per 10,000 in 1891 to 7.1 in 1900.
" Vermont from 5.5 per 10,000 in 1891 to 8.5 in 1900.
" Massachusetts from 6.1 per 10,000 in 1891 to 7.1 in 1900.
" Rhode Island from 5.1 per 10,000 in 1891 to 6.8 in 1900.
" Connecticut from 5.2 per 10,000 in 1891 to 6.6 in 1900.

Various Cities.

" Boston from 6.9 per 10,000 in 1891 to 8.1 in 1900.
" Brussels from 3.4 per 10,000 in 1891 to 4.4 in 1900.
" Breslau from 8.6 per 10,000 in 1891 to 10.8 in 1900.
" Copenhagen from 13.6 per 10,000 in 1891 to 13.9 in 1900.
" Munich from 12.7 per 10,000 in 1891 to 11.9 in 1900 (14.8 in 1897).
" New York from 5.4 per 10,000 in 1891 to 6.7 in 1900.
" Paris from 10.0 per 10,000 in 1891 to 10.5 in 1900.
" St. Petersburg from 9.9 per 10,000 in 1891 to 10.0 in 1900.
" Vienna from 10.4 per 10,000 in 1891 to 12.1 in 1900.

The Relation of Seasons to the Death Rate.—Seasons have an influence upon the mortality of populations. In temperate climates, having a wide difference between the temperature of summer and winter, a very cold winter usually increases the mortality of aged people, while an unusually hot summer increases the infant mortality. The effect of seasons may be shown by dividing the year into four quarters and stating the death rate in each. For this purpose the Registrar-General of England re-estimates the population for each quarter, allowing for increase. Dr. Böckh, of Berlin, makes a new estimate for each month in stating a monthly death rate.

Monthly Deaths in Ninety Cities and Large Towns in Massachusetts in 1901.

	Deaths in each month.	Deaths per day.	Monthly ratio.		Deaths in each month.	Deaths per day.	Monthly ratio.
January	3,742	120.7	108.8	August	3,683	118.8	107.1
February	3,517	125.6	113.2	September	3,514	117.1	105.6
March	3,832	123.6	111.4	October	3,178	102.5	92.4
April	3,406	113.5	102.3	November	3,127	104.2	94.0
May	3,063	98.8	89.1	December	3,296	106.3	95.9
June	2,886	96.2	86.7				
July	3,250	104.8	94.5		40,494	110.9	100.0

In order to show the relative incidence of disease in each month, the writer has adopted the following method, which corrects the effect of the varying length of the months.

Divide the whole number of deaths in the year by 365, to obtain a daily standard (in leap year 366).

Also divide the number of deaths in each month by the number of days in the month.

Divide the daily number of deaths in each month by the daily number for the whole year and multiply by 100.

By this method the intensity of the death rate in each month may be compared with that of the year, and with that of each of the other months.

By quarters of the year the highest mortality in the German Empire, Austria, Switzerland, and France was in the first quarter, but in Italy the highest mortality was in the third quarter. In Massachusetts during the forty years (1856-95) the highest mortality was in the third quarter.

With reference to the different diseases or causes of death considerable variations are found when these causes are compared with each other.

The following table presents the relative monthly incidence in the mortality from eight different diseases in Massachusetts for the twenty years 1876-95. These observations are made from 291,222 deaths from the specified diseases which occurred during the period named (1876-95).

Table showing the Comparative Mortality by Months of each of Eight Diseases in Massachusetts (1876-95).

	Measles.	Scarlet fever.	Diphtheria.	Typhoid fever.	Dysentery.	Cholera infantum.	Consumption.	Pneumonia.
January	94.8	143.2	124.0	79.2	17.9	5.2	104.9	171.4
February	103.4	121.0	106.1	67.3	19.4	4.7	104.2	153.8
March	116.1	129.1	89.4	64.6	19.7	5.3	109.5	158.8
April	166.7	121.5	90.4	67.7	19.8	6.0	110.4	154.5
May	182.9	120.1	92.4	62.8	23.7	9.4	105.6	115.1
June	169.0	91.9	83.7	56.8	35.2	39.5	94.6	60.7
July	128.7	63.9	68.3	64.7	187.9	382.8	93.7	39.0
August	55.2	56.0	65.8	125.0	416.5	443.8	94.2	52.1
September	33.7	55.7	86.3	190.8	282.5	216.2	95.8	39.5
October	30.3	78.8	125.1	181.3	115.5	56.2	95.8	61.8
November	49.7	105.3	134.7	136.4	35.0	12.9	93.8	88.0
December	70.6	114.7	134.1	102.3	18.8	5.5	97.5	128.2
Mean	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

These figures are to be read as follows: Assuming a monthly standard mean of 100 throughout the year, there were 94.8 deaths from measles in January, 103.4 in February, 116.1 in March, etc.

Vital Statistics as Tests of the Comparative Healthfulness of Communities.—1. The general death rate is the test most commonly applied for determining the comparative health of different communities. It, however, has certain limitations. It may be trusted for comparing the health of a city, town, or district for any given year with that of the same community for a preceding year or period. But when comparison with other districts, cities, or towns is to be made, erroneous conclusions may be drawn.

(*a*) Because of differences in the age and sex distribution of the population of the places compared with each other (see page 250).

(*b*) There may be public or private institutions in the city or town in which deaths of persons other than residents occur. Correction for these should be made. For example, in a small town in Massachusetts in 1900 having a population of 3,683, the deaths were 453, giving the enormous death rate of 123 per thousand of the population; 402 of these deaths occurred in a state institution, leaving for the town a death rate of about 19 only.

(*c*) Occupation and social conditions have a decided effect upon the death rate. In the manufacturing communities in which different industries are conducted, one in which the wages are high and the other in which they are low, the death rate of the well-paid population is usually comparatively low.

2. The death rate from the principal infectious diseases is often quoted as an index of sanitary condition, the diseases embraced in such a general statement being measles, diphtheria, scarlet fever, whooping-cough, typhoid

* The figures are from the Mittheilungen aus Kaiserlichen Gesundheitsamte, vii., p. 120, and "Uebersicht über Verbreitung der Krebskrankheit am Ende des 19. Jahrhunderts in einigen ausserdeutschen Gebieten," by Dr. Rahts, and from the Registrar-General's Report upon Cancer in Ireland, Dublin, 1903.

fever, cholera infantum, and tuberculosis. In consequence of the different methods by which such diseases are spread the methods of prevention also differ, and are more susceptible of application in some diseases than they are in others.

For example, a high death rate from typhoid fever in a town would indicate a greater neglect of sanitary precautions than a high death rate from influenza. In presenting the death rates from preventable or communicable diseases it is better to state the death rate of each one separately than to give an average of several, since the latter method is apt to conceal the effects of epidemics from special causes.

3. The infant mortality constitutes a delicate test of sanitary conditions, but should not be quoted as the only test or index. It should always be based upon the number of births, and not upon the census enumeration (see page 251).

4. A more exact method when all the data are complete is to construct a life-table by which the expectation of life may be compared in different districts, as well as among different classes of population. Those of insurance companies may be compared with each other, or with a general average of several companies; but these are obtained from a large number of lives selected by individual examination, and should theoretically give more favorable results than those constructed from the general population. The difference, however, between the expectation of insured lives and that of the general population at the same ages is less than might at first thought have been expected.

These tests of the health of a community, and especially the general death rate, are most trustworthy when the experience of a given community or district for a certain year is compared with its experience in a previous year or number of years, and least trustworthy when comparing its experience with that of other communities or districts.

Effect of Sanitary Improvements upon the Death Rate.—The most convincing proof of the effect of sanitary measures in lowering the death rate is shown in the Reports of the Registrar-General of England, as well as in the Ninth Report of the Privy Council of the same country. In the Registrar's Report for 1881 he says: "There is nothing in the series of reports issued by this office that comes out more distinctly and unmistakably than the wonderful effect which the sanitary operations of the last decade have had in saving life. The Public Health Act came into operation in 1872. The average annual death rate for the immediately preceding ten years (1862–71) had been 22.6, and there were no indications whatsoever of any tendency of the rate to fall lower. Indeed, in 1871, the final year of this period, the rate was exactly the average, viz., 22.6. The act came into force, and at once the rate began to fall, and continued to fall year by year with almost unbroken regularity, until in 1881 it was no more than 18.9. Once only in the ten years that had elapsed since the act came into operation was the rate as high as the average of the previous decades. . . .

"Had the fall in the death rate been limited to a single year or to two years, or even to three, it might have been argued by sceptical persons that the improvement was due to a succession of seasons favorable to health, or to other causes unconnected with sanitary administration, and that the setting in of the fall, coincidently with the coming into operation of public health measures was no more than casual; but, in face of a fall, lasting for ten years in succession and increasing each year in amount, no one can seriously maintain such a position. There can be no real doubt that the saving effected in life was the direct product of the money and labor expended in sanitary improvements."

A similar effect has been observed in many large cities following the introduction of purer water supplies and other sanitary improvements, notably in Hamburg, Paris, Munich, Vienna, Berlin, Chicago, and in Lawrence.

Fallacies in Vital Statistics.—For the purpose of avoiding serious errors in the use and interpretation of vital statistics Quetelet has proposed the following excellent rules:

1. Never have preconceived ideas as to what the figures are to prove.

2. Never reject a number that seems contrary to what you might expect, merely because it departs to a great extent from the apparent average. (Any unusual departure from an apparent average, however, should lead the statistician to make a careful revision of his figures with the object of correcting possible errors.)

3. Be careful to weigh and record *all* the possible causes of an event, and do not attribute to one what is really the result of the combination of several.

4. Never compare data which have nothing in common.

Errors from paucity of data often occur in medical writings where statistics are employed. A small number of observations is not sufficient to establish a conclusion. The degree of approximation to the truth may be estimated by means of Poisson's formula:

μ = the total number of cases recorded in two groups.

m = the number in one group.

n = the number in the other group.

Hence $\mu = m + n$.

The extent of variation in the proportion of each group to the whole will vary within the proportions represented by $\frac{m}{\mu} \pm 2\sqrt{\frac{2mn}{\mu^3}}$, and $\frac{n}{\mu} \pm 2\sqrt{\frac{2mn}{\mu^3}}$.

The larger the number of the total observations (μ) the less will be the value of $2\sqrt{\frac{2mn}{\mu^3}}$, and the less will be the limits of error in the simple proportion $\frac{m}{\mu}$.

Thus, out of 150 cases of diphtheria 18 died, a fatality of 12 per cent. The possible error is determined by the second half of the above formula,

$$\pm 2\sqrt{\frac{2 \times 18 \times 132}{150^3}} = \pm 2\sqrt{\frac{4{,}752}{3{,}375{,}000}} = 0.0756,$$

i.e., the possibility of error = 0.0756 of unity or 7.56 per cent. In other words, in a second series of cases of diphtheria under the same conditions as the foregoing, the fatality may vary from 4.44 to 19.65 per cent., an indefinite result which indicates that the first series cannot be depended upon as establishing more than a *prima-facie* case in favor of any special method of treatment that may have been adopted. If 15,000 cases and 1,800 deaths are taken the limits of error are comparatively small.

The steady decrease in the limits of possible error as the number of recorded facts increases is shown in the following table, where in the first line there are 7 recoveries (70 per cent.) out of 10 cases, and in the last line 700,000 out of a million cases. In the first instance the absurdity of drawing conclusions from a small number is shown, since the possible recoveries are actually greater than the whole number of cases:

Total number of cases.	Number of recoveries.	Possible number recovering out of 100,000 cases according to Poisson's formula.
10	7	29,020 or 110,980.
100	70	57,000 or 83,000.
1,000	700	66,000 or 74,000.
10,000	7,000	68,500 or 71,300.
100,000	70,000	69,600 or 70,400.
1,000,000	700,000	69,870 or 70,130.

An instance illustrating this fallacy occurs in a recent work upon vaccination, in which the author makes the following statement:

A certain Society for the Relief of the Blind publishes the names of fifty people seeking relief, and states the causes of their blindness: "One of these people was blind from having had smallpox. Smallpox hence appears to occasion two per cent. of the blindness at the present time."

The fallacy of this statement appears upon the application of the foregoing rule, since the limits of error

allow a variation of 5.6 per cent. in either direction, or from −3.6 to +7.6 per cent., which renders the observation comparatively valueless. If, on the other hand, the number of the blind were 500,000, and those out of this number whose blindness was caused by smallpox were 2 per cent., or 10,000, the limits of error would only be 0.00056 in either direction, or 0.056 of one per cent., leaving a variation of 9,720 to 10,280 only.

Errors from Incomparability of Data.—The data to be compared should be strictly of a comparable nature. The conclusion that a certain remedy is valuable in the treatment of some definite diseases is not demonstrated by the fact that the fatality in a series of cases thus treated is six per cent., while in another series treated without this remedy it is twelve per cent., unless it is shown that the ages and other previous conditions of the patients in the two cases are not widely different, and unless the numbers constituting the series are sufficiently great to avoid the fallacy due to paucity of data.

Errors from the Composition of Rates.—These are among the most common of all statistical errors, and show the fallacy of dealing with average rates by any shorter method than that of dealing with the sums of the numbers to be compared.

For example, the death rate of Boston in the census year 1900 was 20.81 per one thousand. That of Chelsea was 19.02, of Revere 14.14, and of Winthrop 7.59.

If these death rates are averaged as follows:

20.81
19.02
14.14
7.59
4)61.56
15.39

the resulting death rate of these four municipalities (Suffolk County) is 15.39, and very many instances are to be found in which this erroneous method is employed.

The only correct method of obtaining the combined death rate is as follows:

Cities and towns.	Populations.	Deaths, 1900.
Boston	560,892	11,671
Chelsea	34,072	648
Revere	10,395	147
Winthrop	6,058	46
	611,417	12,512

Therefore $\frac{12,512 \cdot 1,000}{611,417} = 20.46$, the true death rate of the County.

The error arises from the fact that the largest city in the group is given, in the first calculation, only as much prominence in obtaining the result as each of the others, namely, one-fourth of the whole, whereas its population constitutes over ninety-three per cent. of the whole.

Errors from Stating Deaths as a Ratio of the Total Deaths.—There is nothing erroneous *per se* in stating the deaths at any age as a percentage of the total number of deaths, or the deaths from any special cause as a percentage of the deaths from all causes. It is a useful and, in fact, the only method practicable when it becomes necessary to state the proportion of one of these to the other. But beyond this such method cannot be trusted. For example, the proportion of fatal accidents in Massachusetts, in 1900, among boys under five years of age was 14.5 per cent. of all fatal accidents among males, and that of girls of the same age was 24.3 of all fatal accidents of females. From these figures, however, it cannot be inferred that girls are more liable to fatal accidents than boys, since the contrary is the fact, the actual numbers being 205 such deaths among boys under five, and 126 among girls. The only reasonable conclusion is that at higher ages females are much less subject to fatal accidents than males. When stated as a ratio of the living population of the same ages, the deaths by accident of boys under five were fourteen per ten thousand, and those of girls of the same age were only nine per ten thousand.

Life Tables.—The usefulness of life tables is twofold. They constitute the basis of life insurance, and serve as an index of the sanitary condition of the community out of whose data they are constructed.

Life tables differ for the same group of population from year to year, and they also differ when calculated from the statistics of different portions of a group of inhabitants, as, for example, those of a large city, compared with those of any of the outlying districts beyond its borders.

The work of constructing a life-table for any American State or city is necessarily less satisfactory in its results than the work of making a similar table for any of the civilized nations or communities of Europe, since most foreign populations are more stationary than those of America.

The essential data for constructing a life-table are the number, ages, and sexes of the living, and the same data for the dying.

1. Theoretically, the best method of constructing a life-table would be to observe a large number of children, all born on the same day, through life, entering in a column (headed l_x) the number who remain alive at the end of each successive year, until all have died; and in a second colume (d_x) the number dying before the completion of each year of life. Therefore, d_x represents the number out of l_x persons, attaining the precise age x, who die before reaching the age $x+1$. Therefore $d_x = l_x - l_x + 1$, and the number dying between the ages x and $x+1$ is equal to the difference between the numbers living at the ages x and $x+1$. It is not practicable to observe a body of children throughout life in this manner, so that other methods must be adopted.

2. It is not necessary to assume, as in the preceding case, that all the persons have been born on the same day. If we could trace a large number of children throughout life, without reference to the dates of birth, a life-table could be constructed, if the number of the living and dying in each year of life were known.

The great life insurance companies employ a method somewhat similiar to this, in which tables are constructed from the results of watching a large number of insured lives from the time of insurance to death. These, however, differ from the general population, in that they are selected lives, among whom unfavorable risks are weeded out by medical examination. The result of this process does not, however, present such striking differences from the general population as might at first sight be expected.

3. The common method of constructing a life table consists in taking the experience of several years and comparing the numbers of deaths of persons at different ages with the living at the same ages as determined by the census. For example, in the United States, and especially in States where reliable registration of births and deaths is made, the results of the decennial census enumerations may be employed together with the deaths occurring in the intervening years. By this means the disturbing effect of an epidemic year may be minimized. By this method results are obtained which, being wholly based upon recent observations, are more correct than if a million persons were observed from birth to death; since in the latter case the conditions which determined the rate of mortality might, before the whole series became available, have undergone very great changes, which for practical purposes would render the table valueless.

Dr. Farr's English life table No. 3 was based upon the registered deaths in England during the seventeen years 1838–54, and on the two census enumerations of 1841 and 1851. Many other life tables of English cities and districts have been made since that time and were constructed upon similar principles.

The life table constructed by the writer upon the experience of the population of Massachusetts was based upon the deaths which occurred in the five years 1893–

97, and upon the State census of 1895, the middle year of this period.

There are certain conditions which affect the accuracy of life tables, and particularly American life tables, which may be enumerated as follows:

1. *The Influence of Migration.*—The increase or decrease in the population depends upon two factors, migration and the difference between the numbers of births and deaths. In many of the States the gain by immigration is much greater than the gain by natural increase of births over deaths. Moreover, the increase by immigration is not uniform from year to year, nor is it equally distributed at the different age periods, fully one-half of the immigrants being between fifteen and thirty years of age, while the numbers at the extremes of life are comparatively small.

2. *Defects of the Census.*—Mr. H Gannett, in a paper contributed to the American Statistical Association (Publications, vol. iv., p. 99) estimates a "shortage in the census of 1890 of negro children of about a quarter of a million," and of native white children "about the same." If this be correct, the entire shortage in the total population, including that of foreign whites, must leave a million unaccounted for in the United States. In States with complete registration it is possible to supply the deficiency for the first four or five years of life with a reasonable degree of accuracy from the registered births.

3. *The Practice of Incorrectly Reporting the Ages of the Living and the Dead.*—This error is of two kinds: (*a*) Greater numbers of persons are reported at the even ages, 20, 30, 40, etc. (both living and dead) than at 19, 21, 29, 31, etc., in consequence of the common habit of using round numbers instead of accurate ages. This may be partly eliminated by employing the periods 25–35,35–45, etc., instead of 20–30, 30–40, etc. (*b*) The habit especially among unmarried females of understating the ages of the living. This appears to a greater or less degree to be a common practice in all countries where census enumerations are taken.

4. *Defects in Birth and Death Registration.*—These defects depend upon the want of thoroughness with which the laws relating to birth and death registration are executed, and also upon the efficiency of such laws to secure the desired results. In some of the older States the birth and death returns are undoubtedly collected with a reasonable degree of completeness, and in such States life tables may be made from the returns of the whole population.

The following statement by Newsholme in the chapter on vital statistics in his "Hygiene and Public Health" presents in a condensed manner the general principles involved in the construction of a life table:

"It is usual to start with 1,000,000 or 100,000 children at birth and to make a separate table for the proportionate number of males and females at birth. Thus in Brighton in 1881–90 these were in the proportion of $51,195 \times 48,805$. Starting with 51,195 male infants at birth, and multiplying this number by .84608, the probability of surviving one year, we obtain $51,195 \times .84608 = 43,315$. For the second year of life the probability of surviving was .93398; hence the number of survivors is $43,315 \times .93398 = 40,452$, etc. The general arrangement is shown in the preceding example of a life table, which only presents the data at or near the two extremes of life, the intermediate figures having been omitted from considerations of space.

BRIGHTON LIFE TABLE, MALES.

(Based on the mortality of the ten years 1881–90.)

Age. x.	Dying in each year of life. d_x.	Born, and surviving at each age. l_x.	Sum of the number living, or years of life lived at each age, $x+1$, and upward to the last age in the table. Σl_{x+1}.	Mean after life time (expectation of life) at each age. e_x.
0	7,880	51,195	2,206,174	43.59
1	2,863	43,315	2,162,859	50 43
2	996	40,452	2,122,407	52.96
3	733	39 456	2,082.951	53.29
4	440	38,723	2,044,228	53 29
..	....	.....	.....	....
..	....	.....	.....	....
97	12	29	43	1.60
98	7	17	26	1.53
99	4	10	16	1.48

The 43,315 males surviving to the end of the first year of life out of 51,195 born will each have lived a complete year in the first year, or among them 43,315 years. Similarly the 40,452 males will live among them 40,452 further complete years, and so on, until all the males started with become extinct at age 105. Evidently, therefore, the total number of complete years lived by the 51,195 males started with at birth will be $43,315 + 40,452 + 39,456 + 38,723 + \ldots + 10 + 6 + 4 + 3 + 2 + 1 = 2,206,174$ years, this sum being obtained by adding together the numbers living at each age beyond the age in question down to its last item. This number of years is lived by 51,195 males. Hence the number of complete years lived by (*i.e.*, the expectation of life of) each male $= \frac{2,206,174}{51,195} = 43.09$ years. This is termed the *curtate expectation of life.* It deals only with the complete years of life, not taking into account that portion of life time lived by each person in the year of his death, which may be assumed to be, on an average, half a year. Hence the complete expectation of life according to the above table is 43.59 years.

The materials for the construction of a life table are illustrated in the following table, from which the Massachusetts Life Table (1893–97), published in the Thirtieth Annual Report of the State Board of Health for 1898, was constructed:

POPULATION OF MASSACHUSETTS, 1885, AND DEATHS, 1893–97.

Age periods.	Population, 1895.			Deaths, 1893–97.		
	Total.	Males.	Females.	Total.	Males	Females.
0 to 5	*235,647	*118,453	*117,194	78,779	42,710	36,069
5 to 10	224,119	112,296	111,823	6,730	3,345	3,385
10 to 15	202,900	101,574	101,326	3,460	1,655	1,805
15 to 20	225,881	110,565	115,316	6,305	2,899	3,406
20 to 25	265,983	123,692	142,291	9,982	4,899	5,083
25 to 35	465,943	227,630	238,313	20,148	10,103	10,045
35 to 45	341,535	168,997	172,538	18,832	9,610	9,222
45 to 55	245 586	118,417	127,169	19,377	9,895	9,482
55 to 65	157,651	72,766	84,885	22,334	11,278	11,056
65 to 75	90,088	41,040	49,048	25,561	12,694	12,867
75 to 85	35,405	15,460	19,945	20,547	9,675	10,872
85 to 95	6,123	2,180	3,943	7,105	2,713	4,392
Over 95	308	77	231	559	152	407
Age unknown	3,014	1,554	1,460	496	378	118
Total	2,500,183	1,214,701	1,285,482	....	.....	.....

*The population figures in this line (0–5) were not used in the construction of the life table, but the figures employed were estimated from the registered births and the deaths under five years of age.

In the English life tables it has been customary to estimate the population at the middle of a given year for life-table purposes, the census being taken on April 1st. In Massachusetts the census has usually been taken so near the middle of the year (about June 1st), that the slight error arising from the difference between this date and the middle of the year may practically be disregarded.

The deaths in any year are distributed throughout the year, and it is plain that the deaths registered at any age x will not have occurred at the precise age x, but some will have just attained that age, and others will have been close upon $x+1$. Now it is assumed that these deaths at age x occur at equal intervals throughout the ensuing year, an assumption which is approximately correct except for the first two years of life. It is therefore customary to distribute the deaths in the first year of life by months, and then to calculate the mean from this distribution.

Massachusetts Life Table.

(Based on the Mortality of the Five Years 1893–97.)

Table No. 1.—Males.						Table, No. 2.—Females.					
Age.	Dying in each year of age.	Born and surviving at each age.	Population or years of life lived in each year of age.	Years of life lived in and above each year of age.	Expectation of life at each year of age.	Age.	Dying in each year of age.	Born and surviving at each age.	Population or years of life lived in each year of age.	Years of life lived in and above each year of age.	Expectation of life at each year of age.
x.	d_x.	l_x.	P_x.	Q_x.	E_x.	x.	d_x.	l_x.	P_x.	Q_x.	E_x.
0	8,849	51,350	46,343	2,263,907	44.09	0	7,151	48,650	43,907	2,267,469	46.61
1	1,794	42,501	41,604	2,217,564	52.18	1	1,662	41,499	40,668	2,223,562	53.58
2	818	40,707	40,298	2,175,960	53.48	2	763	39,837	39,455	2,182,894	54.79
3	559	39,889	39,609	2,135,662	53.54	3	544	39,074	38,802	2,143,439	54.83
4	424	39,330	39,118	2,096,053	53.29	4	385	38,530	38,337	2,104,637	54.62
5	316	38,906	38,748	2,056,935	52.87	5	318	38,145	37,986	2,066,300	54.17
6	252	38,590	38,464	2,018,187	52.30	6	250	37,827	37,702	2,028,314	53.62
7	205	38,338	38,235	1,979,723	51.64	7	206	37,577	37,474	1,990,612	52.97
8	170	38,133	38,048	1,941,488	50.91	8	170	37,371	37,286	1,953,138	52.26
9	146	37,963	37,890	1,903,440	50.14	9	147	37,201	37,127	1,915,852	51.50
10	123	37,817	37,755	1,865,550	49.33	10	129	37,054	36,990	1,878,725	50.70
11	110	37,694	37,639	1,827,795	48.49	11	113	36,925	36,868	1,841,735	49.88
12	104	37,584	37,532	1,790,156	47.63	12	113	36,812	36,755	1,804,867	49.03
13	111	37,480	37,424	1,752,624	46.76	13	123	36,699	36,637	1,768,112	48.18
14	135	37,369	37,301	1,715,209	45.90	14	146	36,576	36,503	1,731,475	47.34
15	159	37,234	37,154	1,677,899	45.06	15	172	36,430	36,344	1,694,972	46.53
16	181	37,075	36,984	1,640,745	44.26	16	195	36,258	36,160	1,658,628	45.74
17	195	36,894	36,796	1,603,761	43.47	17	206	36,063	35,960	1,622,468	44.99
18	211	36,699	36,593	1,566,965	42.70	18	218	35,857	35,748	1,586,508	44.24
19	226	36,488	36,375	1,530,372	41.94	19	230	35,639	35,524	1,550,760	43.51
20	241	36,262	36,141	1,493,997	41.20	20	241	35,409	35,288	1,515,236	42.79
21	255	36,021	35,893	1,457,856	40.47	21	251	35,168	35,042	1,479,948	42.08
22	268	35,766	35,632	1,421,963	39.76	22	255	34,917	34,790	1,444,906	41.38
23	280	35,498	35,358	1,386,331	39.05	23	261	34,662	34,531	1,410,116	40.68
24	289	35,218	35,073	1,350,973	38.36	24	265	34,401	34,268	1,375,585	39.99
25	296	34,829	34,781	1,315,900	37.67	25	269	34,136	34,001	1,341,317	39.29
26	301	34,633	34,482	1,281,119	36.99	26	274	33,867	33,730	1,307,316	38.60
27	305	34,332	34,179	1,246,637	36.31	27	278	33,593	33,454	1,273,586	37.91
28	309	34,027	33,872	1,212,458	35.63	28	282	33,315	33,174	1,240,132	37.22
29	313	33,718	33,560	1,178,586	34.95	29	286	33,033	32,890	1,206,958	36.54
30	316	33,403	33,245	1,145,026	34.28	30	290	32,747	32,602	1,174,068	35.85
31	318	33,087	32,928	1,111,781	33.60	31	294	32,457	32,310	1,141,466	35.17
32	319	32,769	32,609	1,078,853	32.92	32	297	32,163	32,014	1,109,156	34.48
33	319	32,450	32,290	1,046,244	32.24	33	301	31,866	31,715	1,077,142	33.80
34	320	32,131	31,971	1,013,954	31.56	34	302	31,565	31,414	1,045,427	33.12
35	322	31,811	31,650	981,983	30.87	35	306	31,263	31,110	1,014,013	32.43
36	325	31,489	31,326	950,333	30.18	36	308	30,957	30,803	982,903	31.75
37	328	31,164	31,000	919,007	29.49	37	312	30,649	30,493	952,100	31.06
38	331	30,836	30,670	888,007	28.79	38	315	30,337	30,180	921,607	30.38
39	334	30,505	30,338	857,337	28.10	39	318	30,022	29,863	891,427	29.69
40	337	30,171	30,002	836,999	27.41	40	320	29,704	29,544	861,564	29.00
41	341	29,834	29,662	796,997	26.72	41	324	29,384	29,222	832,020	28.31
42	346	29,493	29,320	767,334	26.02	42	326	29,060	28,897	802,798	27.62
43	352	29,147	28,971	738,014	25.32	43	329	28,734	28,570	773,901	26 93
44	359	28,795	28,615	709,043	24.62	44	332	28,405	28,239	745,331	26.24
45	368	28,436	28,252	680,428	23.93	45	335	28,073	27,905	717,092	25.54
46	379	28,068	27,878	652,176	23.24	46	346	27,738	27,565	689,187	24.85
47	393	27,689	27,492	624,298	22.55	47	354	27,392	27,215	661,622	24.15
48	410	27,296	27,091	596,806	21.86	48	367	27,038	26,854	634,407	23.46
49	429	26,886	26,671	569,715	21.19	49	379	26,671	26,481	607,553	22.78
50	448	26,457	26,233	543,044	20.58	50	395	26,292	26,094	581,072	22.10
51	466	26,009	25,776	516,811	19.87	51	410	25,897	25,692	554,978	21.43
52	483	25,543	25,301	491,035	19.22	52	423	25,487	25,275	529,286	20.77
53	502	25,060	24,809	465,734	18.58	53	437	25,064	24,845	504,011	20.11
54	520	24,558	24,298	440,925	17.95	54	457	24,627	24,398	479,166	19.46
55	539	24,038	23,768	416,627	17.33	55	476	24,170	23,932	454,768	18.81
56	561	23,499	23,218	392,859	16.72	56	494	23,694	23,447	430,836	18.18
57	585	22,938	22,645	369,641	16.11	57	512	23,200	22,944	407,389	17.56
58	608	22,353	22,049	346,996	15.52	58	530	22,688	22,423	384,445	16.95
59	636	21,745	21,427	324,947	14.94	59	550	22,158	21,883	362,022	16.34
60	659	21,109	20,780	303,520	14.38	60	572	21,608	21,322	340,139	15 74
61	677	20,450	20,111	282,740	13.83	61	588	21,036	20,742	318,817	15.16
62	691	19,773	19,427	262,629	13.28	62	606	20,448	20,145	298,075	14.58
63	709	19,082	18,727	243,202	12.75	63	625	19,842	19,530	277,930	14.01
64	729	18,373	18,008	224,475	12.22	64	644	19,217	18,895	258,490	13.45
65	748	17,644	17,270	206,467	11.70	65	665	18,573	18,240	239,505	12.90
66	769	16,896	16,511	189,197	11.20	66	689	17,908	17,563	221,265	12.36
67	789	16,127	15,732	172,686	10.71	67	715	17,219	16,861	203,702	11.83
68	810	15,338	14,933	156,954	10.23	68	743	16,504	16,132	186,841	11.32
69	827	14,528	14,114	142,021	9.78	69	771	15,761	15,375	170,709	10.83
70	840	13,701	13,281	127,907	9.34	70	793	14,990	14,593	155,334	10.36
71	845	12,861	12,438	114,626	8.91	71	800	14,197	13,792	140,741	9.91
72	847	12,016	11,592	102,188	8.50	72	821	13,388	12,977	126,949	9.48
73	842	11,169	10,748	90,596	8.11	73	825	12,567	12,154	113,972	9.07
74	831	10,327	9,911	79,848	7.73	74	824	11,742	11,330	101,818	8 67
75	816	9,496	9,088	69,937	7.36	75	818	10,918	10,509	90,488	8.29
76	794	8,680	8,283	60,849	7.01	76	806	10,100	9,697	79,979	7.92
77	769	7,886	7,501	52,566	6.67	77	790	9,294	8,899	70,282	7.56
78	741	7,117	6,746	45,065	6.33	78	768	8,504	8,120	61,383	7.22
79	707	6,376	6,022	38,319	6.01	79	742	7,736	7,365	53,263	6.89
80	672	5,669	5,333	32,297	5.70	80	711	6,994	6,638	45,898	6.66
81	632	4,997	4,683	26,964	5.40	81	678	6,283	5,944	39,260	6.25
82	590	4,365	4,070	22,281	5.10	82	640	5,605	5,285	33,316	5.94
83	465	3,775	3,502	18,211	4.82	83	600	4,965	4,665	28,031	5.65
84	499	3,229	2,980	14,709	4.56	84	559	4,365	4,085	23,366	5.65
85	452	2,730	2,504	11,729	4.30	85	518	3,806	3,547	19,281	5.07

MASSACHUSETTS LIFE TABLE.—*Continued.*

Table No. 1. Males.

Age.	Dying in each year of age.	Born and surviving at each age.	Population or years of life lived in each year of age.	Years of life lived in and above each year of age.	Expectation of life at each year of age.
$x.$	$d_x.$	$l_x.$	$P_x.$	$Q_x.$	$E_x.$
86	402	2,278	2,072	9,225	4.05
87	353	1,876	1,700	7,153	3.81
88	307	1,523	1,370	5,453	3.58
89	263	1,216	1,084	4,083	3.36
90	220	953	843	2,999	3.15
91	181	733	642	2,156	2.94
92	146	552	479	1,514	2.74
93	116	406	348	1,035	2.55
94	88	290	246	687	2.37
95	66	202	169	441	2.18
96	48	136	112	272	2.00
97	33	88	71	160	1.82
98	23	55	43	89	1.62
99	15	32	24	46	1.44
100	9	17	13	22	1.29

Table No. 2.—Females.

Age.	Dying in each year of age.	Born and surviving at each age.	Population or years of life lived in each year of age.	Years of life lived in and above each year of age.	Expectation of life at each year of age.
$x.$	$d_x.$	$l_x.$	$P_x.$	$Q_x.$	$E_x.$
86	476	3,288	3,050	15,734	4.79
87	434	2,812	2,595	12,684	4.51
88	333	2,378	2,181	10,089	4.33
89	351	1,985	1,810	7,908	3.98
90	310	1,634	1,479	6,098	3.73
91	270	1,324	1,189	4,619	3.49
92	232	1,054	938	3,430	3.25
93	194	822	725	2,492	3.03
94	160	628	548	1,767	2.81
95	120	468	403	1,219	2.60
96	100	339	289	816	2.41
97	77	239	200	527	2.20
98	55	162	134	327	2.02
99	40	107	87	193	1.80
100	27	66	53	106	1.58

MASSACHUSETTS LIFE TABLE.

Table No. 3.

(Based on the Mortality of the Five Years 1893–97.)

Age. $x.$	$m_x.$ Annual Mortality per Unit at Each Year of Age.		$P_x.$ Probability of Living One Year from Each Age.	
	Males.	Females.	Males.	Females.
0	0.19095	0.16287	0.82569	0.84939
1	.04313	.04087	.95778	.95995
2	.02030	.01933	.97990	.98085
3	.01411	.01403	.98599	.98607
4	.01084	.01004	.98922	.99001
5	.00815	.00835	.99188	.99168
6	.00655	.00663	.99347	.99339
7	.00536	.00550	.99464	.99452
8	.00447	.00456	.99556	.99546
9	.00386	.00396	.99616	.99606
10	.00326	.00349	.99675	.99652
11	.00292	.00306	.99709	.99695
12	.00277	.00307	.99722	.99693
13	.00297	.00336	.99703	.99665
14	.00362	.00400	.99640	.99601
15	.00428	.00473	.99573	.99528
16	.00489	.00539	.99511	.99461
17	.00530	.00573	.99471	.99429
18	.00577	.00610	.99425	.99392
19	.00621	.00647	.99381	.99356
20	.00667	.00683	.99335	.99320
21	.00710	.00716	.99292	.99286
22	.00752	.00733	.99251	.99268
23	.00792	.00756	.99212	.99249
24	.00824	.00773	.99179	.99230
25	.00851	.00791	.99153	.99212
26	.00873	.00812	.99131	.99192
27	.00892	.00831	.99112	.99170
28	.00912	.00850	.99092	.99154
29	.00933	.00870	.99072	.99134
30	.00950	.00890	.99054	.99114
31	.00966	.00910	.99039	.99094
32	.00978	.00928	.99026	.99077
33	.00988	.00949	.99017	.99055
34	.01001	.00961	.99004	.99043
35	.01017	.00984	.98988	.99021
36	.01037	.01000	.98968	.99005
37	.01058	.01023	.98948	.98982
38	.01079	.01044	.98927	.98962
39	.01101	.01063	.98905	.98942
40	.01123	.01083	.98881	.98923
41	.01150	.01109	.98857	.98897
42	.01180	.01128	.98827	.98878
43	.01215	.01152	.98792	.98855
44	.01255	.01176	.98753	.98831
45	.01302	.01200	.98706	.98802
46	.01359	.01255	.98650	.98773
47	.01430	.01301	.98581	.98708
48	.01513	.01367	.98498	.98643
49	.01608	.01431	.98404	.98579
50	.01708	.01514	.98307	.98498

Age. $x.$	$m_x.$ Annual Mortality per Unit at Each Year of Age.		$P_x.$ Probability of Living One Year from Each Age.	
	Males.	Females.	Males.	Females.
51	0.01808	0.01596	0.98208	0.98417
52	.01909	.01674	.98109	.98340
53	.02023	.01759	.97997	.98256
54	.02140	.01873	.97888	.98144
55	.02268	.01989	.97758	.98031
56	.02416	.02107	.97613	.97915
57	.02583	.02231	.97450	.97793
58	.02757	.02364	.97280	.97664
59	.02968	.02513	.97075	.97518
60	.03171	.02683	.96878	.97353
61	.03366	.02835	.96689	.97205
62	.03557	.03008	.96505	.97037
63	.03786	.03200	.96285	.96850
64	.04048	.03408	.96032	.96648
65	.04331	.03646	.95761	.96419
66	.04657	.03923	.95449	.96152
67	.05015	.04241	.95107	.95848
68	.05424	.04606	.94719	.95498
69	.05859	.05015	.94307	.95108
70	.06325	.05434	.93869	.94710
71	.06794	.05866	.93430	.94301
72	.07307	.06327	.92951	.93867
73	.07884	.06788	.92406	.93435
74	.08385	.07273	.91953	.92983
75	.08979	.07784	.91407	.92508
76	.09586	.08312	.90852	.92020
77	.10252	.08877	.90248	.91500
78	.10984	.09458	.89588	.90969
79	.11740	.10075	.88911	.90408
80	.12601	.10711	.88146	.89834
81	.13496	.11406	.87357	.89209
82	.14496	.12110	.86483	.88581
83	.15591	.12862	.85536	.87915
84	.16745	.13684	.84549	.87192
85	.18051	.14604	.83440	.86390
86	.19402	.15607	.82314	.85523
87	.20765	.16724	.81188	.84567
88	.22469	.18019	.79850	.83470
89	.24271	.19392	.78356	.82322
90	.26097	.20960	.76915	.81028
91	.28193	.22708	.75290	.79607
92	.30480	.24733	.73551	.77989
93	.33333	.26759	.71430	.76399
94	.35772	.29197	.69655	.74522
95	.39053	.32010	.67324	.72406
96	.42857	.34602	.64706	.70502
97	.46479	.38500	.62286	.67715
98	.53488	.41045	.57798	.65044
99	.62500	.45977	.52381	.62617
100	.69230	.50943	.48572	.59399

One hundred thousand infants, followed through their first year of life in the period 1893-97, in Massachusetts, yielded 90,250 years of life. To obtain this mean of the infants living throughout the first year, the following method was employed:

All of the deaths of infants under one month old which occurred in the years 1893-97 were tabulated from the mortality returns in the office of the secretary of state, also those of infants who died in the second and the third months of life separately, then those of infants who died in the three succeeding months of life (fourth to sixth) in one group, and then those who died in the succeeding six months in another group. From these data, and from the births registered in the five years ending with June 30th, 1897, the figures for the first year of life were calculated after the method shown by Dr. Farr in his life table No. 3, page xxiii.

The foregoing mean, 90,250 (46,343 males and 43,907 females) (the arithmetical mean of the series l_0, $l_{\frac{1}{12}}$, $l_{\frac{2}{12}}$, . . . l_1), is used as the first term of column P (see foregoing table, p. 260). All of the succeeding terms in the column for the years 1, 2, 3, 4, etc., are the means of the terms in the preceding column l_x, using the formula,

$$P_x = \frac{l_x + l_{x+}}{2}.$$

In these tables Column x presents the ages from birth up to one hundred years.

Column d_x presents the numbers of those dying in each age of life.

Column l_x, Table 1, presents the survivors out of 51,350 males at birth at each age of life. (The females were 48,650, which added to the number of males makes 100,000.)

Column P_x presents the population maintained by the numbers in column l_x, beginning with 46,343 males (and 43,907 females), in all 90,250 persons.

Column Q_x shows the aggregate number of years which the persons at each age in the table will live, until their extinction by death.

Column $E_x = \frac{Q_x}{l_x}$ is the mean future life time of the persons living at each age in the table, the expectation of life.

In the third table, the mortality column presents the mortality per unit of the population at each age of life, the figures being obtained by dividing the deaths at each age by population at such ages, the proper corrections and interpolations having been made, either by the analytical method described by Dr. Farr in his English Life Table, No. 3, p. xxv., or by the less accurate method known as the graphic method described by Mr. George King in the *Journal of the Institute of Actuaries* (October, 1883) and in Newsholme's "Vital Statistics," 3d edition, p. 266. From this column (m_x) the probability of living at each year of age (p_x) is obtained by the formula $p_x = \frac{2 - m_x}{2 + m_x}$ applied to each year of the series.

Column l_x is obtained by the formula $l_x \times p_x = l_x + 1$, and column P_x is obtained by the formula $\frac{l_x + l_{x+1}}{2}$.

From these tables it appears that, out of 100,000 children born alive in Massachusetts during the years 1893–97, 16,000 or nearly one-sixth die before arriving at the age of one year; 78,963 or nearly four-fifths attain the age of three years; 77,051 survive the age of five years, or seventy-seven per cent.; 50,124 or a little more than one-half attain the age of fifty-three years; 24,993 or nearly one-fourth live to the age of seventy-two years.

These figures present very decided differences as compared with those which were published for the same State in 1855 by Mr. E. B. Elliott.* In that report it was shown that the numbers dying before the close of the first year out of 100,000 born were 15,510, or nearly the same as those for the year 1895 for the same age. At the end of three years the survivors were only 74 per cent instead of 79 per cent. as in 1895, and one-half had died before the close of the forty-first year, instead of surviving to the fifty-third as in 1895.

Since the numbers of each sex are unequal at birth, the males continue in greater numbers until the fifty-third year, when the greater death rate of the males has reduced their number below that of the females, and the females continue in excess throughout the remainder of life. Observing the tables more closely, it appears that the comparative intensity of the death rate of the sexes varies at different points of the table. For the first five years the death rate of males exceeds that of females. From age five to age nineteen inclusive the rate of females exceeds that of males, and from age twenty to the end of life the death rate of females is less than that of males.

In table 3 are presented two columns, in which are shown the probability of living one year from each age and the mortality per unit of the population at each year. At birth the probability of living a year is for males 0.82569 and for females 0.84939, that of boys at birth being about the same as for men of eighty-six, and that of girls about the same as that of women at eighty-six or eighty-seven. The probability of living a year is at its highest point for boys at age twelve (0.99722) and for girls it is about the same for age eleven as for age twelve (0.99695 and 0.99693).

A comparison of death rates at different periods presents certain points worthy of notice.

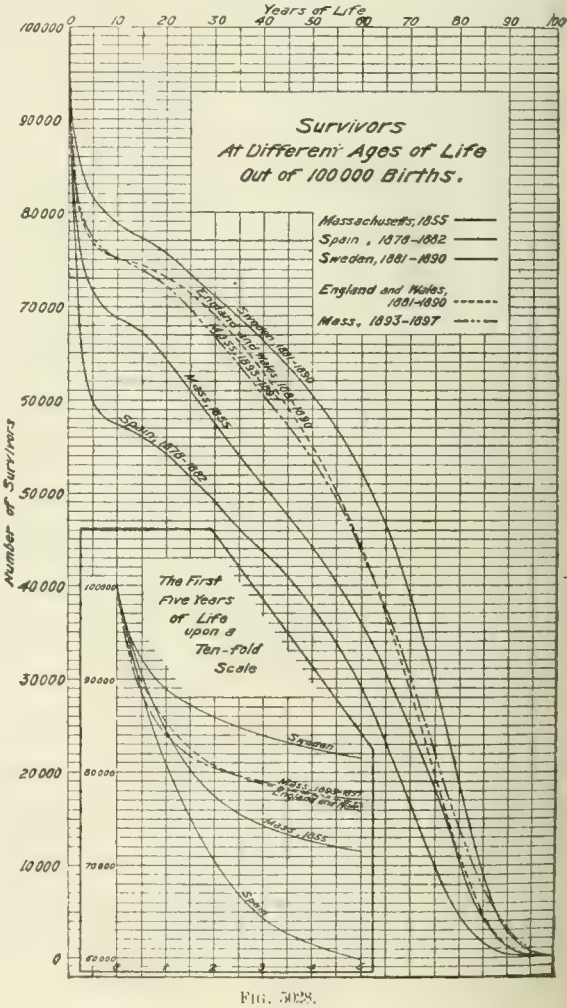

FIG. 5028.

* Sixteenth Registration Report, Massachusetts, 1857.

DEATH RATES AT DIFFERENT AGES OF LIFE, MASSACHUSETTS, AT TWO PERIODS, 1865 AND 1895.

Ages.	1865.	1895.	Ages	1865.	1895.
All ages	20.64	19.0	30-40	11.7	9.7
Under 5	68.6	64.5	40-50	11.9	12.6
5-10	9.6	6.2	50-60	17.5	20.4
10-15	5.1	3.2	60-70	32.9	39.4
15-20	9.6	5.3	70-80	70.5	82.4
20-30	12.6	7.1	All over 80	168.2	184.6

The death rate of children under five, and especially of those under one year of age, has not undergone very marked changes, but that of all ages from five to forty has very perceptibly diminished, while that of ages above forty has increased. This result has been produced by the great reduction in the number of deaths from infectious diseases, including consumption, which occur in the early period of life, from two years up to thirty. By this means a much larger ratio of the population than formerly survives to live throughout the useful and wage-earning period of life. This causes a material increase in the number of years lived at the later ages of life.

These persons being spared from the diseases incident to childhood naturally increases the relative mortality from the diseases of adult life and old age.

This decided increase in the number of survivors throughout the useful ages of life has a marked effect upon the vitality of the population. It is undoubtedly due in no small degree to the increased attention which has everywhere been given in the past twenty-five years to public hygiene.

The accompanying diagram represents the numbers of survivors at the different ages of life in Sweden, England, Spain, and Massachusetts out of 10,000 at birth. Those of Massachusetts are presented for two periods 1893–97 and 1855, showing the marked changes which have taken place. Sweden is selected because it has a low death rate and is often selected as a standard of a healthy population. Spain, on the contrary, has a high death rate, which is chiefly due to excessive mortality in the early years of life. (See table on p. 264 and diagram on p. 262.)

In consequence of the close contiguity of the lines in

PRINCIPAL VITAL STATISTICS OF THE SIX NEW ENGLAND STATES, FOR THE NINE YEARS 1892–1900.

Mean annual population of the period (estimated).	MAINE, 680,961.		NEW HAMPSHIRE, 397,294.		VERMONT, 339,121.		MASSACHUSETTS, 2,564,484.		RHODE ISLAND, 393,784.		CONNECTICUT, 840,789.		TOTAL NEW ENGLAND, 5,216,433.	
	Number.	Rate.	Number.	Rate.	Number.	Rate.	Number.	Rate.	Number.	Rate.	Number.	Rate.	Number.	Rate.
Marriages and rate per 1,000 population	49,706	8.11	35,385	9.90	25,481	8.45	205,738	8.91	30,925	8.72	59,084	7.81	406,319	8.66
Living births and rate per 1,000 population	127,954	20.88	73,554	20.58	62,904	20.61	630,798	27.33	92,200	26.02	177,700	23.48	1,165,110	24.82
Deaths and rate per 1,000 population	100,334	16.37	64,419	18.02	50,716	16.62	434,604	18.83	67,331	19.00	132,175	17.46	849,579	18.09
Deaths under one year and rate per 1,000 births	15,364	120.10	10,766	146.40	8,753	139.10	98,662	156.40	15,415	167.20	26,880	151.30	175,840	150.90
Deaths from consumption, and rate per 10,000 population	10,471	17.09	6,095	17.05	4,619	15.13	48,890	21.18	7,366	20.78	12,421	16.41	89,862	19.14
Deaths from pneumonia, and rate per 10,000 population	9,029	14.73	6,273	17.54	5,091	16.68	43,252	18.74	6,279	17.72	11,664	15.41	81,588	17.38
Deaths from typhoid fever, and rate per 10,000 population	2,015	3.29	994	2.78	952	3.12	6,242	2.70	1,025	2.89	2,126	2.81	1,354	2.84
Deaths from smallpox, and rate per 10,000 population	5	.008	0	0	1	.003	65	.03	7	.02	26	.03	104	.02
Deaths from measles, and rate per 10,000 population	331	.54	156	.44	172	.56	1,527	.66	532	1.50	800	1.06	3,518	.75
Deaths from scarlet fever, and rate per 10,000 population	367	.60	327	.91	278	.91	3,969	1.72	684	1.93	933	1.23	6,558	1.40
Deaths from diphtheria and croup, and rate per 10,000 population	1,582	2.58	1,035	2.89	970	3.18	12,765	5.53	1,793	5.06	3,514	4.64	21,659	4.61
Deaths from cholera infantum, and rate per 10,000 population	5,006	8.17	3,597	10.06	1,626	5.33	22,520	9.76	4,460	12.57	7,613	10.06	44,822	9.55
Deaths from cancer, and rate per 10,000 population	1,470	7.39	2,430	6.80	2,001	6.56	15,532	6.73	2,188	6.17	4,328	5.72	30,949	6.59

INTERNATIONAL VITAL STATISTICS.

Births per 1,000 of the Population in Certain Countries.

	England and Wales.	Scotland.	Ireland	Denmark.	Norway.	Sweden.	Austria.	Hungary.	Switzerland.	German Empire.	Holland.	Belgium.	France.	Spain.	Italy.
Average of twenty-five years, 1875–1899	32.3	32.2	23.8	31.3	30.7	28.7	38.0	42.9	28.9	37.2	34.7	30.1	23.7	35.6 *	36.6
1900	28.7	29.6	22.7	29.8	30.1	26.9	...	39.3	28.6	35.6	31.5	28.9	21.4	34.4	32.9

Deaths per 1,000 of the Population in Certain Countries.

Average of twenty-five years, 1875–1899	19.3	19.4	18.1	18.5	16.7	17.1	28.8	32.7	20.8	24.4	20.6	20.3	22.0	30.4 *	26.7
1900	18.2	18.5	19.6	16.9	15.8	16.8	....	26.9	19.3	22.1	17.8	19.3	21.9	29.4	23.7

Marriage Rates (1900). (Persons Married per 1,000 of the Population.)

1900	16.0	14.6	9.6	15.3	13.9	12.3	....	17.7	15.5	17.0	15.2	17.2	15.5	17.7	14.3

* Spain, average of twelve years (1888–99).

the first five years of life, the figures for the first five years are given upon a separate diagram, in which the divisions representing the age periods are increased tenfold.

The preceding tables present the Vital Statistics of the six New England States, for the nine years 1892–1900. The populations which are given for each State, and for the whole district, are the mean annual populations of the nine-year period.

The Tables of International Vital Statistics contain the birth and death rates for the twenty-five years, 1875–'99, and for the year 1900, and the marriage-rates (persons married per 1,000 living) for the year 1900 in the principal countries of Europe.

DATA FOR CONSTRUCTION OF DIAGRAM OF SURVIVORS. TABLE SHOWING SURVIVORS AT DIFFERENT AGES OF LIFE OUT OF 10,000 BORN.

	Sweden ‡ 1881-90.	England and Wales—* 1881-90.	Massachusetts— 1893 97.	Massachusetts—† 1855.	Spain—‡ 1878-82.
0	10,000	10,000	10,000	10,000	10,000
1	8,895	8,536	8,100	8,449	8,083
2	8,586	8,067	8,054	7,733	7,060
3	8,399	7,878	7,896	7,424	6,433
4	8,258	7,758	7,786	7,258	6,151
10	7,882	7,495	7,516	6,873	5,747
15	7,713	7,423	7,394	6,726	5,602
20	7,551	7,281	7,213	6,437	5,413
25	7,338	7,090	6,959	6,100	5,164
30	7,109	6,844	6,674	5,748	4,908
35	6,876	6,550	6,372	5,408	4,596
40	6,628	6,216	6,054	5,078	4,378
45	6,349	5,839	5,721	4,748	4,088
50	6,043	5,405	5,355	4,409	3,765
55	5,687	4,891	4,918	4,022	3,381
60	5,239	4,275	4,390	3,597	2,914
65	4,658	3,534	3,759	3,065	2,327
70	3,900	2,684	3,029	2,475	1,666
75	2,948	1,786	2,207	1,833	997
80	1,872	970	1,411	1,059	465
85	894	388	759	437	149
90	275	100	320	118	40
95	....	14	92	20.5	....
100	....	9	14	2.2	....

* Fifty-fifth Report of Registrar-General, Supplement, vol. i., p. xiv.; vol. x., part i., p. 75.

† Sixteenth Registration Report, Massachusetts, 1857.

‡ Bulletin de l'institut international de statistique.

Samuel W. Abbott.

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VITILIGO.—This affection of the skin, which is likewise known by the name of leucoderma, consists in the development of whitened areas upon various portions of the body, but especially upon the face, neck, and hands. It is due to localized loss of pigment in rounded or ovoid patches of various size, having sharply defined margins and surrounded by more or less deeply pigmented skin which gradually shades off into the normal. The characteristic features of the whitened spots are, that their border is usually convex, giving the impression that they extend into their darkened surroundings, or that, in their advance, they drive the pigment before them; that there is no change in the structure, sensations, or secretions of the affected areas; and that their tendency is to persist and to increase in extent, being little affected by any treatment. It is an acquired condition which comes on usually in youth or early adult life without previous ill health or prodromes, although in some instances it has been known to follow local injury; and sometimes it develops in the neighborhood of a pigmented mole. The dark-skinned races are rather more subject to vitiligo than those of fair skin and light hair, and it is not so very rarely seen in the negroes of this country, in whom the contrast between the perfectly white spots and the normal skin produces a striking effect. I have seen instances in which much discomfort of mind was occasioned by the fact that the white patches were merging into each other until extensive regions of the body had lost their pigment, and the negro was fearful that he was "turning into a white man." The hair may lose its pigment in the same way as the skin, and rounded or irregular tufts of gray may appear upon the head. In white races the affected regions are often more noticeable in the summer time, when the surrounding pigmentation becomes deeper

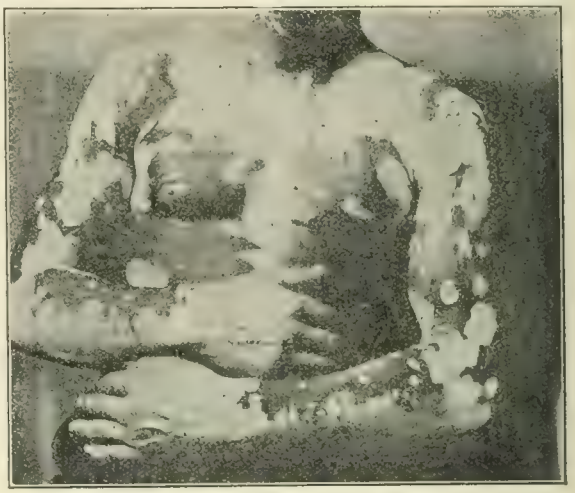

FIG. 5029.—Vitiligo.

The *diagnosis* of vitiligo is not difficult, although it is liable to be confounded with morphœa, chloasma, tinea versicolor, syphilitic pigmentations, macular leprosy, and albinism. One chief point by which it is distinguished from other conditions is the normal condition of the skin, apart from its loss of pigment. In morphœa there are structural changes. In tinea versicolor the patches are inflammatory and itchy, and from them there can be scraped scales which show, under the microscope, the characteristic groups of spores, although, when circumscribed areas of healthy white skin are enclosed in the brownish patches of this disease, vitiligo may be closely simulated; but the margins will be found irregular instead of clean-cut. In chloasma there is increased pigmentation of the patch itself and the circumference is the part which appears white. The distinction has been made that in vitiligo the margin of the white area is convex toward that which is pigmented, while in chloasma it is concave; but in some instances the patches run together in such a way that this distinction becomes more theoretical than apparent. Syphilitic pigmentations, especially about the neck in women, may persist after other manifestations have disappeared and may, in some instances, be mistaken for vitiligo. In the macular form of lepra the patches of white skin have an irregular outline, not so abrupt as in vitiligo, and the tinge is rather grayish than dead white; then, too, the skin is either thickened or atrophied and anæsthesia or impaired sensation is present. Finally, in albinism we have, as in vitiligo, an absence of normal pigment, but in the former it is a congenital defect and the whole surface of the body, including the hair and eyes, may be devoid of pigment.

The *pathology* of vitiligo is obscure. Leloir has described a parenchymatous neuritis in which the axis cylinder had disappeared, the myelin sheath had broken down, and the nerve fibre had become transformed into an empty primitive sheath, whose nuclei had proliferated. The affection begins as a hyperpigmentation in areas which run into one another and assume a polycyclic character, the pigment becoming absorbed from the centre and deposited in excess in the marginal epidermis, the connective-tissue cells, and about the vessels and hair follicles.

The *etiology* of vitiligo is not well understood, but the cause of the condition is usually ascribed to perverted innervation. It is probable that the disappearance of the pigment from one spot and its increased deposit in a neighboring part is due to atrophy in the former and to hypertrophy in the latter, both changes being effected through the agency of the sympathetic nervous system. Sometimes, though rarely, the proper proportion of pigmentation is spontaneously restored, but in the majority of instances the affected areas tend to increase in extent and the condition to assume marked chronicity. When large areas of surface are involved the term leucoderma becomes appropriate.

The *treatment* is unsatisfactory. Some reports of success from electricity have been made. Local applications for the removal of surrounding pigmentation are resorted to with the view of rendering the white regions less noticeable. The internal administration of nerve tonics, especially strychnine and arsenic, has been advised. Blistering the patches to excite a deposit of pigment has been tried, but the results are not brilliant. If the spots are located upon the face or other exposed part, artificial staining may be employed, and dyes used to restore the color of the hair. *Charles Warrenne Allen.*

VITREOUS BODY OR HUMOR.—Anatomy.—The vitreous body is a transparent, semifluid, colorless mass, of soft gelatinous consistence, subglobular in form, which fills the posterior four-fifths of the interior of the eyeball; it is bounded by the optic-nerve entrance and retina behind, by the retina on each side, and in front by the lens and its suspensory ligament which fit into a depression known as the patellar fossa. It serves as a support to the tunics of the eyeball, and, of lesser importance, as a clear refractive medium; its index of refraction is slightly greater than that of distilled water. Chemically, it consists of 98.5 per cent. water and 1.5 per cent. solids.

There has been much discussion regarding the structure of the vitreous. When the fresh substance is thrown upon a muslin filter, the greater part passes through as a watery liquid, a very small proportion remaining behind—demonstrating the existence of a *supporting framework* and a fluid portion. It is quite generally held that there is a very delicate fibrillar *reticulum*, in which are scattered a few round or branched cells of the connective-tissue type, most abundant in the periphery, and often a variable number of migratory leucocytes. The cells are known as *vitreous corpuscles;* they are often difficult to recognize; they are peculiar in exhibiting large vacuoles which push the nucleus to one side, and in presenting a number of budlike swellings (Fig. 5030).

The vitreous body is enclosed in a delicate, structureless, glassy membrane, the *hyaloid membrane*, which lies in close apposition with the entire inner surface of the retina; it can be readily separated from the latter, except posteriorly where the retinal vessels of fœtal life have entered, and anteriorly at the patellar fossa. At the ora serrata, the hyaloid membrane splits into two layers: the first, the hyaloid membrane proper, exceedingly delicate, which is continued over the anterior surface of the vitreous body; and the second, which blends with the posterior layer of the suspensory ligament of the lens.

The central portion of the vitreous body is penetrated by a channel (*hyaloid canal, canal of Stilling, canal of Cloquet, central canal*); this is filled with fluid, is limited by a wall of extremely delicate homogeneous membrane, and extends from the disc to the posterior pole of the lens; it is about 2 mm. in diameter, with a slight dilatation at both ends. This canal conveys the hyaloid branch of the central artery to the lens during fœtal life; in the adult it forms part of the posterior lymph passages of the eyeball, having its outlet in the lymph spaces of the optic nerve.

The adult vitreous has no blood-vessels, its nourishment being received from the surrounding structures, particularly the uvea; hence diseases of the retina, choroid, and ciliary body almost always implicate the vitreous. Vitreous humor is never regenerated after loss; the diminution in volume is compensated for by the addition of aqueous. If the escape of vitreous is small, no injurious effects follow; if large, the consequences are serious—the globe softens, shrinkage results, and sight is lost.

Diseases of the Vitreous Body.

Congenital Anomalies.—1. *Persistent Hyaloid Artery.*—During fœtal life the hyaloid artery, a branch of the central artery of the retina, passes through the central canal of the vitreous from the optic-nerve entrance to the posterior pole of the lens; it usually begins to shrivel during the sixth month and has generally disappeared at the end of fœtal life. Sometimes this process of obliteration fails, and a greater or lesser remnant of the artery persists during life. This can be seen with the ophthalmoscope as a grayish cord or thread which arises from the optic disc and stretches into the vitreous for a variable distance; it may terminate by a free extremity in the vitreous, or may traverse the latter and be attached to the posterior pole of the lens, the attachment to the lens being marked by a small opacity (congenital posterior polar cataract); or the thread may be attached to the lens with its free end floating in the vitreous; or the vestige may be represented by an irregular, minute deposit of connective tissue upon the disc. In rare instances the persistent artery continues to carry blood. Vision is generally good, but sometimes such eyes are amblyopic or present other congenital defects.

2. *Opacity of the Walls of the Hyaloid Canal.*—In unusual instances the walls of the hyaloid canal are abnormally opaque, causing some interference with central acuteness of vision; this anomaly is visible with the ophthalmoscope as a grayish, tubular cord extending from disc to lens.

Hyalitis (*Inflammation of the Vitreous*).—This term includes two types: first, a purulent inflammation (*suppurative hyalitis*), and second, a form characterized by the occurrence of *opacities in the vitreous.* As will be

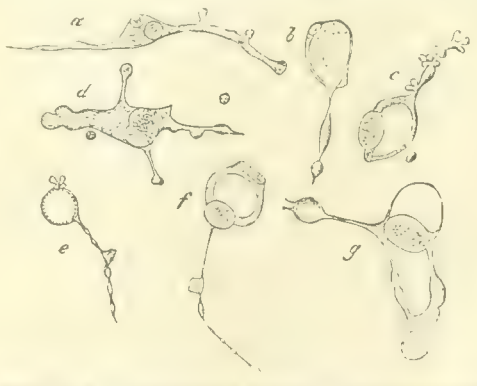

Fig. 5030.—Cells of the Vitreous Humor. Schwalbe.) *a* and *d* without vacuoles; *b*, *c*, *e*, *f*, *g*, vacuolated.

readily understood by considering the avascular and almost structureless nature of this tissue, inflammations of the vitreous are rarely primary; they generally accompany or are the result of inflammation of the retina and uveal tract.

Suppurative hyalitis is an infective inflammation of the vitreous, which is generally merely part of a purulent choroiditis or panophthalmitis. It is caused by *infection*, the result of a penetrating wound, a foreign body, or an iridochoroiditis following an operation upon the globe; it may arise in the course of the exanthemata, erysipelas, relapsing fever, meningitis and cerebro-spinal meningitis, infective blood diseases, and lengthy debilitating fevers; it may follow metastatic choroiditis after inflammation of the cord in the newly born child.

Since the affection is generally secondary to inflammation of other structures, symptoms of the primary disease will be present, such as posterior synechiæ and other evidences of iridocyclitis. If the media are clear, the purulent exudate is readily seen as a yellowish reflex shining through the pupil, and the ophthalmoscope detects the presence of an opaque mass which may be circumscribed, but is usually diffuse.

When it is more or less circumscribed, the condition presents appearances which are very much like those of glioma of the retina, and as a matter of fact it is known as *pseudoglioma*. It can generally be distinguished from a true glioma by the history of the case, by the presence of the signs of iritis or uveitis, and by the diminished tension. The disease tends to run a chronic course. In rare instances, when circumscribed, and especially when of traumatic origin, purulent hyalitis may leave a more or less useful eyeball. But in the great majority of cases, and in every instance in which panophthalmitis exists, sight is lost; the retina becomes detached, the soft eyeball shrinks, and an atrophied globe results; enucleation then becomes necessary, especially if the shrunken organ menaces the safety of the other eye. No method of treatment will prevent such a result. If, during the course of a debilitating fever, suppurative hyalitis is detected early, it may be possible to save some vision in the affected eye by vigorous supporting treatment of the general condition. Intra-ocular injections of chlorine water have been recommended (Berry).

Opacities in the Vitreous may be fixed, but they are usually movable. They vary in size from fine dust-like deposits (*hyalitis punctata*) to large masses. They may have any shape: dust, specks, threads, flakes, bands, or irregular membranous masses. They may be entirely free or may present one or more attachments to enveloping tunics. In the great majority of instances the affection is secondary to diseases of neighboring structures.

The opacity causes an impairment of the transparency of the vitreous. It can be detected with the ophthalmoscope held at a distance, the patient moving the eye in various directions and then fixing it. Under such circumstances the opacity, if movable, will be seen as a dark object behind the pupil, upon the red background of the fundus, and will disappear from view as it falls to the bottom of the vitreous. The rapidity of movement depends upon the consistence of the vitreous. If this is normal, the movement is slow; if it is fluid, the movement is rapid. By placing a $+4$ D. lens in the sight hole of the ophthalmoscope and getting closer to the patient, then increasing the strength of the lens to $+16$ D. and simultaneously approaching the eye, successive depths of the vitreous chamber can be focussed and explored. With minute or very delicate opacities, faint illumination and the plane mirror of the ophthalmoscope should be employed.

Opacities of the vitreous are distinguished from opacities of the cornea and lens by their depth, their mobility, the gradual settling after the eye has been moved and is then steadied, and by the fact that they cannot be seen by oblique focal illumination. Patches of choroidal pigment are differentiated in like manner by dissimilarity in shape, and by difference in depth as measured by their refraction.

If the symptoms due to disease of the surrounding structures be excluded, the subjective manifestations of opacity of the vitreous are the occurrence of one or more spots in the field, and more or less impairment of vision, the degree of the latter depending upon the size, situation, and density of the opacity; patients may merely complain of motes but slightly more pronounced than the muscæ volitantes of normal eyes, or the vision may be almost or completely abolished. When the opacity is situated deeply in the vitreous, the annoyance of the patient is increased by the shadow which the opacity throws upon the retina. Very often the patient will cast the opacity out of the line of vision by a sudden movement of the eyes or head, and thus obtain unobstructed vision for a moment; in other cases vision will be improved after the eyes have been kept quiet for a time, thus allowing the opacity to settle. The disease must not be confounded with muscæ volitantes; the latter are described below.

Opacities in the vitreous are very common. In most instances they depend upon some disease of the choroid, ciliary body, or retina. They are frequently found in high degrees of myopia associated with choroidal disease, and are then often seen as flakes and threads. They are not uncommon in syphilitic chorioretinitis and cyclitis, in such cases being usually dustlike, with or without threadlike or shredlike additions. They result from hemorrhages into the vitreous, and when thus produced they may constitute membranous masses; occasionally the latter are attached to the retina and are accompanied by the formation of new blood-vessels, constituting *retinitis proliferans*. In some cases errors of refraction are found in the eyes which are the seat of opacities of the vitreous; but there is no evidence that the two anomalies bear any etiological relationship except in myopia. Very often the condition results from retinal or choroidal disease, depending upon some disturbance of the general health, of which the following are the most common examples: Disturbances of menstruation, disorders of the liver, debilitating diseases, endarteritis, gout, malaria, and the effects of the prolonged use of arsenic. Finally, it is not uncommon to find opacities of the vitreous, of various shapes and sizes, in apparently normal eyes of healthy individuals; in such cases no cause can be assigned. *Asteroid hyalitis* is the name given by Benson to a very rare condition, probably congenital, in which the vitreous is filled with minute, light-colored spheres.

Treatment consists in an attack upon the causative disease. In syphilitic cases the usual treatment of this infection, especially if the mercury be given hypodermically, will often cause a clearing up. Disturbances of the system should be corrected by appropriate means. High myopia requires proper correction with glasses, and careful attention to general and ocular hygiene. Where no cause can be assigned, good results sometimes follow the use of iodides, with or without mercury in small doses. Small quantities of jaborandi or pilocarpine, or larger hypodermic doses of the latter, are useful, followed by hot baths, so as to produce diaphoresis, if the patient is able to tolerate such vigorous treatment. Abstraction of blood from the temples and the local application of the galvanic current have been reported of benefit.

Large membranous deposits that persist after every other method of treatment has failed, may sometimes be divided with a narrow knife or a knife-needle, providing no active disease of neighboring parts exists and there is no blood-vessel formation. The instrument is inserted in front of the equator of the eyeball, just below the lower border of the external rectus muscle. In some cases the result of this operation has been to cause a shrinking of the opacity and an improvement of vision.

While in syphilitic cases, in examples of hemorrhages of small size, and in a few others in which the opacities are of limited extent and of delicate consistence, complete absorption takes place after some months, in most of the instances of this condition disappearance is incomplete or the opacities are permanent. There exists also a tendency to recurrence after complete or incomplete absorption. Not uncommonly, when extensive opacities are attached to surrounding structures, shrinkage takes place, the retina becomes deprived of its natural support and becomes detached.

Muscæ Volitantes (*Myodesopsia*) are the black specks or motes often seen in the field of vision, especially when the eye is directed toward the light or a bright surface. They are most often complained of by myopes. They are caused by the shadows which the cells and migratory leucocytes of the vitreous cast upon the retina. These shadows usually have the shape of dots or small bubbles, isolated or collected into strings or clusters; less frequently they are of larger, fantastic shapes. Any movement of the eye sets them in motion. After the eye ceases to move, they continue to float across the field, gradually settling out of the line of vision. This phenomenon may be produced entopically by partially closing the lids or by looking through a small opening in a card, and by facing the light or a white surface. It is often seen while looking into the tube of a microscope.

Muscæ are not true opacities of the vitreous, and consequently cannot be detected with the ophthalmoscope. They are normal phenomena, occurring in healthy eyes, perfectly transparent, and not disturbing to vision. Present in all eyes, they are usually disregarded. When noticed they cause annoyance and often anxiety, which is apt to be aggravated by the habit of the patient of searching for them. Neither must they be confounded with scotomata, which are blind spots in the field of vision, due to a loss of function of certain portions of the retina.

Many of the patients who complain of muscæ have some error of refraction. The correction of the latter often gives relief. In any case the patient should be assured that the occurrence is devoid of significance. He will then cease to look for the shadows, and in consequence will no longer be annoyed by them.

Blood-vessel Formation in the Vitreous (*Retinitis Proliferans*).—Occasionally we observe dense grayish or bluish-white membranes, provided with new blood-vessels, which have no apparent connection with the retinal vessels, attached to the retina in the situation of the optic-nerve entrance, projecting into the vitreous, and hiding a portion of the fundus. These represent the sequels of previous pathological processes—either hyalitis, or hemorrhages, or chronic retinal inflammation. Examples of the last cause have been associated with general disease (syphilis, nephritis, diabetes, gout). The pathology is obscure. There is interference with vision, the degree depending upon the density, size, and position of the membrane. The tissue is incapable of absorption.

Hemorrhages into the Vitreous.—These are usually due to rupture of some of the vessels of the ciliary processes or of the choroid, less frequently to a break in the retinal vessels, in consequence of injury, vascular disease, or alterations in the blood. Anæmia, nephritis, diabetes, arteriosclerosis, myopia, glaucoma, and menstrual disturbances are predisposing factors. There are also some examples, generally in young male adults, in which hemorrhage into the vitreous occurs *spontaneously*, and often repeatedly. Such cases have been attributed to irregularities of the circulation and to gout.

If the hemorrhage be recent and slight, a bright red reflex is seen with the ophthalmoscope; if greater, dark red masses are observed, which may appear red at the margins; if considerable, a large part or all of the vitreous chamber is filled, and no fundus reflex is obtained. There is always impairment of vision, but the degree varies with the amount and situation of the extravasation. With large hemorrhages sight is immediately reduced to perception of light.

Small hemorrhages are often absorbed after some weeks or months with restoration of good vision. Not infrequently, however, the process of absorption is incomplete and opacities remain. Large extravasations usually leave dense membranous opacities which cause serious impairment of vision. Such hemorrhages necessarily produce considerable disorganization of the vitreous structure, followed by fluidity, and not infrequently by detachment of the retina.

If these hemorrhages are seen early, treatment consists in absolute bodily rest with the head in an elevated position, cold compresses on the closed lids, the administration of cardiac sedatives and ergot, and abstraction of blood from the corresponding temple. Subsequently small doses of potassium iodide and mercury, pilocarpine sweats, saline cathartics, hot compresses to the closed lids, and subconjunctival injections of saline solution may be used to promote absorption. Attention to the general health, avoidance of the stooping posture, and rest of the eyes are also indicated. Large membranous, non-vascular opacities may be cut with a knife-needle or a narrow knife after all inflammation has subsided and no tendency to recurrence of hemorrhage appears to exist.

Degenerations of the vitreous comprise: (1) Synchysis; (2) sparkling synchysis; (3) fatty degeneration; (4) detachment; (5) ossification.

Synchysis (*fluidity of the vitreous*) is a softened or fluid condition of the vitreous. This can be diagnosticated with certainty only when vitreous opacities exist and move with undue rapidity during motions of the eyeball. The condition is often accompanied by tremulousness of the iris; but this symptom may exist without fluid vitreous, and is no proof of the existence of synchysis. It is merely an evidence that, owing to relaxation or rupture of the suspensory ligament, the iris has been left without the support of the lens upon which it usually depends. The tension of the eyeball is commonly diminished, but it may be normal, or even increased, as in certain cases of glaucoma.

Synchysis occurs with high degrees of myopia, with or without complicating choroiditis and posterior staphyloma; with extensive vitreous opacities; after ocular injuries with extensive hemorrhage into the vitreous; and with degenerative processes of the eye in general. In such cases the loss in consistence depends upon an impairment of nutrition. Advanced age is a predisposing factor. Fluid vitreous is not infrequently present in eyes that have never suffered from any disease, and in which no definite cause can be assigned.

No treatment is of any avail. Recognition of the condition is of practical importance when an operation upon the globe, such as cataract extraction, or iridectomy for glaucoma is contemplated, since it forms a complicating circumstance and increases the liability to loss of vitreous.

Synchysis scintillans (*sparkling synchysis*) is the name given to a fluid vitreous which presents numerous small crystals of cholesterin and tyrosin. These are seen to move rapidly whenever the eye moves, reflecting the light of the ophthalmoscope, and giving rise to a beautiful picture which resembles a shower of brilliant sparks. These crystals are supposed to represent a degenerative change of blood effused into the vitreous at some previous period, or else decomposition of the wandering cells. The condition is not of common occurrence. It is usually found in old persons, and is said to be more common among alcoholics, in those suffering from some general disease of nutrition, and in choroiditis. But clinically it is met with most frequently in eyes which are apparently healthy in other respects. There is usually little or no reduction of vision if the eye is otherwise normal. Such individuals sometimes complain of seeing glittering flashes when the eye is moved. The condition is not amenable to treatment.

Detachment of the vitreous is a serious condition which, if it ever exists alone, cannot be recognized clinically. The support which the vitreous usually gives is withdrawn, and the retina becomes detached. This condition follows traumatism, especially perforating wounds, also cataract extraction, choroiditis, intra-ocular hemorrhages, intra-ocular growths, high degrees of myopia, and extensive staphylomata. After loss of a considerable portion of the vitreous from any cause, there is shrinkage, detachment of the hyaloid, followed by that of the retina. Detachment is not amenable to any form of treatment. If the eye remains quiescent, no interference is called for. If symptoms of irritation, pain, or sympathetic disease set in, enucleation is indicated.

Fatty degeneration of the vitreous is occasionally met

with as an evidence of senile decay. The patient complains of muscæ volitantes, and the ophthalmoscope reveals numerous white glistening spots evenly distributed through the vitreous and having a very limited amount of motion when the eye is moved. There is some reduction in the acuteness of vision. The condition does not call for any special treatment.

Ossification of the vitreous has been described by Wittich and Virchow as a rare form of degeneration, always associated with phthisis bulbi following a suppurating process or hyalitis. The vitreous body changes into a solid fibrous mass of cord-like shape, enlarged at either end. The osseous tissue is developed in the anterior end of this cord. The occurrence of this change is doubted by many authorities.

Parasites in the Vitreous.—The presence of entozoa in the vitreous is exceedingly rare except in north Germany. In nearly every instance the parasite has been the *cysticercus cellulosæ*. The filaria sanguinis hominis has been seen in the vitreous, with certainty, in only a single instance. The parasite found in the vitreous is the scolex of the *tænia solium*, the eggs of which enter the circulation from the stomach, and are deposited in the eye between the choroid and the retina. Perforating the latter it escapes into the vitreous.

When still situated between the choroid and the retina it can be seen with the ophthalmoscope as a bluish-gray opacity resembling detachment of the retina. After entering the vitreous, if still alive, it appears as a pale bluish or bluish-gray cyst from which there projects a short white neck and a head. The latter is provided with minute suckers, which can sometimes be seen to move. When this picture is found, particularly when the head is observed to move independently of motions of the eyeball, the diagnosis can be made with certainty. Very often, however, opacities of the vitreous are present and render the diagnosis more difficult. After the death of the parasite it becomes covered with lymph and thus hidden from view with the ophthalmoscope.

Unless removed while still beneath the retina, there is gradual loss of sight and finally destruction of the eyeball. When discovered early, before the entozoon has escaped into the vitreous, it may be removed by forceps through an incision in the sclera. Quite a number of such operations have been successful and have resulted in the preservation of good vision. After the parasite has entered the vitreous it may also be removed, but then the preservation of sight cannot be hoped for. If the attempt at removal be unsuccessful, enucleation is indicated. *Charles H. May.*

VIVISECTION.—According to the definition given in the Century Dictionary, vivisection is the "dissection of a living body; the practice of anatomizing alive, or of experimenting upon living animals for the purpose of investigating some physiological function or pathological process which cannot well be otherwise determined. Vivisection strictly includes only cutting operations; but the term is extended to any physiological experimentation upon living animals. . . . Vivisection in competent and humane hands, under proper and reasonable restrictions, is fruitful of good results to the sciences of physiology and pathology."

The necessity for resorting to this mode of experimentation depends on the fact that physiology, pathology, therapeutics, and bacteriology deal with the phenomena of life, and in order to study them successfully the necessary investigations must be made during the life of the animal upon which experiments are made.

The valuable results which have been attained by such experiments constitute a large share of the actual knowledge now possessed in these departments of medical science. The study of the functions of circulation, respiration, digestion, the nervous system, the investigation of infectious diseases, the reproduction of bone, the action of drugs and poisons and their uses and antidotes have all been greatly facilitated by means of vivisection.

The discovery of the true nature of rabies, of anthrax, glanders, tuberculosis, the Texas cattle fever, and of hog cholera, is due very largely to the assistance afforded by animal experimentation. In the production of a constant supply of diphtheria antitoxin (which has saved thousands of human lives), animal experimentation must necessarily be resorted to. At a hearing before a legislative committee in 1901, which was considering the propriety of legislation to restrict this practice, a witness said: "No father whose child had been saved by such means would care how many lives of animals had been sacrificed in the discovery. We cannot use the rabbit as a unit in estimating the value of our children's lives."

In a lecture before the Royal Society of England, Huxley stated "that the discoveries made by Pasteur alone by means of experimentation upon living animals would have sufficed to pay the war indemnity paid by France to Germany." By means of inoculations practised as the result of Pasteur's experiments, the loss from anthrax in France alone had diminished from ten per cent. in sheep and five per cent. in cattle to less than one per cent. in sheep and one-fourth of one per cent. in cattle.

Galen, Harvey, John Hunter, and others made use of this method in early times, but it has come largely into use in the last half of the nineteenth century.

Like very many practices vivisection is liable to abuse, but, as Bishop Lawrence, of Massachusetts, stated before a legislative committee in 1900, the subject "can be left, with perfect confidence on the part of the community, to a profession that has shown itself worthy of such confidence in its attitude toward humanity, as well as toward the lower animals."

Within the past thirty years vigorous opposition has been made, either to prevent vivisection or to restrict it by law. Scarcely a year now passes in which such restrictive legislation is not proposed in some form or other in one or more States of the Union.

In order to obtain an expression of opinion with reference to the practice of vivisection, a circular was issued by the American Humane Association in 1895, and sent to many prominent physicians, clergymen, educators, and others, and the replies from these sources were classified as follows:

Replies from Physicians.

	Total number.	Per cent.
For vivisection without restriction	220	19.1
For vivisection restricted by utility	513	44.6
For vivisection without pain	186	16.2
For total prohibition of vivisection	207	18.0
Obscure or evasive	24	2.1
Total	1,150	100.0

Replies from Other Professional Men.

	Clergymen.	Educators.	Authors, editors, etc.	Per cent.
For vivisection without restriction	0	34	4	4.7
For vivisection restricted by utility	189	84	63	41.2
For vivisection without pain	116	49	26	23.5
For total prohibition of vivisection	144	52	30	25.7
Obscure or evasive	6	16	2	2.9
Total	455	235	125	100.0

Thus far, while much legislation upon this subject has been proposed, not very many laws have been enacted. After a parliamentary investigation in England a law was enacted in 1876 entitled "An Act to Amend the Law Relating to Cruelty to Animals" (Chapters 77, 39, and 40, Victoria). This act has twenty-two sections, and prohibits the performance of painful experiments on animals except under restrictions; with penalties of not over £50 for the first offence and not over £100 for the second offence.

By Section 3 of this act it is provided that:

1. The experiment must be performed with a view to the advancement of science by discovery of physiological knowledge, or of knowledge which will be useful for the saving or prolonging of life or of alleviating suffering.

2. The experiment must be made by licensed persons.

3. The animal must be under the influence of an anæsthetic.

4. The animal must be killed if pain is likely to continue, or if serious injury is done to the animal.

5. The experiment is not to be performed in illustration of lectures.

6. It is not to be performed for the purpose of attaining manual skill.

By Section 4 the use of urari is prohibited.

By Section 5 restriction is made as to experiments upon dogs, cats, horses, mules, and asses.

By Section 6 public exhibition of such experiments is made illegal.

Other sections relate to the registration and licensing of persons desirous of making experiments and the method of instituting legal proceedings.

The provisions of the act do not apply to invertebrate animals.

By several definite exceptions the restrictions in Section 3, clauses, 1, 3, 4, and 5, are very much modified.

In a recent suit for libel, in England, it was shown that Dr. Bayliss, professor of physiology at London University, was charged by Hon. Stephen Coleridge with cruelty in the conduct of certain physiological experiments. Dr. Bayliss was licensed to perform such experiments under the English act here referred to. Dr. Bayliss sued Mr. Coleridge for libel, won his suit, and was awarded £2,000 damages (*Boston Medical and Surgical Journal*, November 26th, 1903).

Although legislation has been proposed in many States, there are but three in which the statutes contain any reference to vivisection. These are New York, New Jersey, and California. The law of New York respecting cruelty to animals runs as follows:

"If any person shall torture, torment, deprive of necessary sustenance . . . or needlessly mutilate or kill, or cause or procure" the same to be done, to "any living creature, every such offender shall for every such offence be guilty of a misdemeanor."

Following this section there is a paragraph relating to vivisection:

"Nothing in this act contained shall be construed to prohibit, or interfere with, any properly conducted scientific experiments or investigations, which experiments shall be performed only under the authority of the faculty of some regularly incorporated medical college or university of the State of New York."[1] In California the law is substantially the same.[2]

Construing these sections together, according to a familiar legal principle, the law in New York and California regarding vivisection may be stated as follows: Vivisection is lawful when performed under the authority mentioned and when "properly conducted." If improperly conducted, that is, with the infliction of needless or unjustifiable suffering, the offender would be guilty of a misdemeanor, which is punishable in New York by fine or imprisonment, or both, the maximum penalty being one year in the county jail, including thirty days of solitary confinement, and a fine of $250. In California, also, fine and imprisonment may be imposed for this offence. Vivisection undertaken without the authority prescribed in the statutes is punishable in like manner.

In New Jersey the law and the penalty are substantially the same, except that the authority under which vivisection may there be performed, if "properly conducted," is that of any "incorporated medical society of the State."[3]

In all the other States, with few exceptions—and the exceptions, doubtless, will soon disappear—there are laws against cruelty to dumb animals. In these States, therefore, vivisection—at least such vivisection as is performed without the use of anæsthetics—might or might not be adjudged to come within the statute. In each case there would be a question whether suffering had been inflicted needlessly or cruelly, and each case would be decided according to its own circumstances and to the views of the particular tribunal before which it came. In the interest both of the medical profession and of dumb animals, it is to be hoped that the statute of New York will be copied by all the States, and it would be well if the law were somewhat extended. In Great Britain the buildings in which vivisection may be performed are licensed, and there is an inspector to see that the provisions of the statute are carried out. In this way, additional precautions are taken. It is scarcely necessary to point out that such regulations do not hamper the competent and conscientious surgeon, and that they tend to make vivisection legally possible everywhere, because they render it free from objection in the view of the people generally.

Henry Childs Merwin.

Revised by *Samuel W. Abbott.*

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VOICE AND SPEECH. See *Larynx, Physiology of.*

VOLITION, DISORDERS OF. See *Insanity.*

VOLVULUS. See *Colon* (*Surgical*) and *Intestinal Obstruction.*

VOMITING. See *Emetics*, and *Stomach, Diseases of.*

VOMITING OF PREGNANCY.—By way of introduction it may be assumed that no more common source of discomfort, distress, and even danger besets the condition of pregnancy than the symptom which serves as the subject of this article. It may be asserted, also, that very few who have not experienced it have any adequate idea of how distressing it may, and often does, become. It is doubtless a fact that the nausea accompanying, or at times taking the place of, the actual vomiting is of such intensity, is of such a sickening and depressing character, is so much worse than the ordinary and commonplace nausea due to other causes, as to be to many the hardest to bear of all the trying experiences of the process of maternity.

At other times, it must be admitted, the vomiting is easy, accompanied by little if any nausea, and it is a noticeable fact that even in some cases in which vomiting has been frequent and persistent for months the patients have held their flesh and strength to a wonderful degree. In these latter cases the body must hold its own with a very meagre supply of food, for to a casual observer it would appear that none is retained.

It has been customary to draw a line of demarcation between the slight and the severe cases, or between those which are rebellious to treatment and threaten life and those which do not. The former have been called the "physiological" or "simple" vomiting of pregnancy; the latter the "pernicious," or "incoercible," or "uncontrollable" vomiting of pregnancy. The correctness of these descriptive terms will be called in question elsewhere.

On the other hand, Dr. Graily Hewitt has very properly pointed out the important distinction which exists between the vomiting *of* pregnancy and the vomiting *dur-*

ing pregnancy, the latter being merely an accidental occurrence in the course of pregnancy, while the former is a direct result from the fact of pregnancy.

As regards the history of this troublesome complication, it is probably the history of the human race, for from the nature of the case it must have been a frequent symptom during pregnancy at a very early period in the history of the world. What Hippocrates and other ancient worthies have to say upon the matter, however, is of far less importance than the fact that so many men in the present day show plainly by their writings how little they understand either the cause or the treatment of the trouble. The very multiplicity of theories as to the cause, and of remedies for working a cure, serves as a sufficient commentary upon the unsettled state of medical opinion upon one of the most common and important symptoms which the physician is called upon to treat. It does not seem right that so simple and every-day an experience as the vomiting of pregnancy should remain at the present day a matter of mystery, and that its treatment should continue so unsatisfactory, uncertain, and often futile. The writer believes that most cases may be explained according to a very simple theory, and his experience demonstrates that treatment along that same line may be confidently expected to give prompt and complete relief in the vast majority of cases.

Symptoms.—The most common form of this complaint is the occurrence of one or more attacks of vomiting directly after rising from bed in the morning. This may end the attack for the day, or the vomiting may recur during breakfast as well as at intervals throughout the day. So frequent is this experience on rising that the affection has come to be universally known as "morning sickness."

At times vomiting is absent, but the patient experiences attacks of nausea instead. Either the nausea or the vomiting may begin before rising, at times even awaking the patient from her sleep, and may then recur as above stated.

In the severer forms of pregnancy vomiting every attempt to take food is followed by fresh paroxysms, and indeed, not infrequently, vomiting is wellnigh constant, irrespective of anything which is taken into the stomach. The symptoms may be so urgent that sleep is prevented, nutrition wholly fails, loss of flesh and strength is rapid, elevation of temperature, small and rapid pulse, delirium and death supervene, all in the course of a few weeks.

It has been customary to divide these severe cases, commonly known as the pernicious vomiting of pregnancy, into three stages. During the first stage the symptoms develop with more or less rapidity, as a rule giving no indication of the gravity of the situation which is to follow until, after a period varying from a few days to several weeks, the vomiting becomes so frequent and so urgent as materially to affect the patient's strength. The threatening aspect of the case now visibly augments from day to day. Nothing whatever is retained upon the stomach, and, in default of food or drink, vomiting of mucus, bile, and even blood continues at short intervals.

No one can now overlook the serious nature of the complication. Suffering and anxiety are plainly depicted in the patient's face, the pulse has already become markedly accelerated, and then, with the advent of fever, is ushered in the second stage.

In this stage the temperature remains persistently above 100° F., the pulse varies from 100 to 140 per minute, the skin is hot and dry except that in some cases the extremities remain cold and clammy. Thirst is a prominent symptom, the mouth is parched and dry, the tongue may be cracked, and sordes may appear upon the teeth. Ptyalism and jaundice are commonly present. The urine is scanty, often albuminous and tinged with bile. As a rule, diarrhœa exists.

With the onset of the third stage most of these symptoms abate, the patient being able once more to take and retain small amounts of food. The friends and even the physician may be deceived, thinking convalescence about to be established, while in fact this is merely the period of grave disturbance of the nerve centres preceding death. Delirium is present, with loss of one or more of the special senses. Neuralgic pains are commonly present. The pulse remains between 120 and 140. Coma gradually supervenes and continues until death.

The period of pregnancy at which nausea or vomiting most frequently occurs is during the first six or eight weeks, though they may appear at any time up to delivery. One case is reported in which the patient was married on Monday, began vomiting on the following Saturday, and was delivered normally at such a time as to establish the fact that conception immediately followed marriage. It is probable, however, that discomfort is first noticed, in the majority of cases, somewhere near the end of the first month of pregnancy. Beginning as a slight nausea on rising in the morning, or at the breakfast table, it may go on to the serious train of symptoms described above, or after a few days may wholly disappear. Usually the experience is one of annoyance rather than of actual suffering, and rarely continues after the fourth month.

Diagnosis.—The points involved in the diagnosis are, *first*, to determine the fact of pregnancy; *second*, to decide whether the vomiting is due to the pregnancy or is simply incidental to it—in other words, whether we have to deal with the "vomiting *of* pregnancy" or the "vomiting *during* pregnancy"; and perhaps I may be permitted to add, *third*, to ascertain the local cause of the vomiting.

It is by no means easy to establish the fact of pregnancy at an early stage, and indeed it is often impossible. Until after the first catamenial period has passed it must be chiefly a matter of inference, based upon the opportunity which has been afforded for pregnancy to occur, and upon the possibility or otherwise of the vomiting being due to other causes. As soon as one menstrual period has passed, or when other signs of pregnancy have been discovered, the diagnosis may be made to rest upon a surer basis.

The difficulties in the way of deciding the second point in diagnosis are usually less marked. The peculiar characteristics of pregnancy vomiting are usually sufficiently well marked; yet in some cases it may be necessary to avail one's self of an eliminative diagnosis, making careful examination for disease of stomach, liver, kidney, or other organ which might be productive of the symptoms, and failing to find such cause the diagnosis must rest upon the pregnancy as responsible.

The diagnosis of the abnormal conditions which serve as a cause for the vomiting will be considered under the next heading.

Cause.—Here we reach the great point of difference which exists between observers, and yet the point upon which it is most important that definite and correct views should exist, for upon it must rest the most successful treatment. It has been customary to attribute the vomiting to a reflex irritation proceeding in some mysterious way from the developing ovum, but more stress has commonly been laid upon the condition of the patient, whether as concerning her stomach or her nervous system, which made this irritation potent for evil, than upon the source of irritation itself. Moreover, as regards the nature of this irritation, men have held, and hold today, most divergent views, though it is coming to be admitted more and more generally that its origin is to be found in some abnormal pelvic condition.

My own preference is to consider that a number of causes may operate in different cases, or even in the same case, to produce the symptoms, and these causes should be classified as predisposing and exciting.

As to the predisposing causes, the chief is undoubtedly that state of exalted nervous sensibility which shows itself in so many and in such unmistakable ways during pregnancy. It is a matter of universal observation that trifling emotions, whether of fright, grief, annoyance, or otherwise, produce in the pregnant woman results far surpassing those which she would ordinarily experience. Similarly, it is doubtless true that conditions giving rise

to irritation of sensory nerve fibres may produce correspondingly exaggerated results in the way of reflex phenomena.

Undoubtedly an important factor in this connection lies hidden in racial conditions. In no other way can we adequately explain the fact that Carl Braun, in his enormous experience, has never met with a fatal result, nor even with a case sufficiently serious to require induced abortion, while in France, England, and America a fatal termination is far from being a rarity. Hirst, in his "System of Therapeutics," shows a mortality of ninety-five in two hundred and thirty-nine cases reported.

Other factors may possibly be found in the hydræmic condition of the blood; the condition of fear, or at least the state of introspection and anticipation in which so many newly pregnant women find themselves; the various functional perversions of taste, smell, appetite, and digestion; and lastly, and more generally, in the presence of gastric catarrh in more or less marked degree.

Far more important, however, are the exciting causes which, as has already been suggested, will usually be found in some abnormal condition of the pelvic organs.

The theory which has been held in favor the longest is perhaps that of Bretonneau, who considered that the distention of the body of the uterus by the growing ovum caused pressure upon or tension of the nerve filaments, so setting up a reflex irritation. To a superficial observer this serves as a very satisfactory explanation, yet it fails utterly in many cases and must be rejected as inadequate. This distention occurs in every case, and yet many escape the nausea altogether, while others have it in one pregnancy and not in another. Moreover, the symptoms cease in most cases while this distention is still going on, and often the cessation is sudden and complete.

Another theory rests upon the supposition of metritis; yet metritis is more common in those who have borne children, while the vomiting of pregnancy is more common in primiparæ.

Still others, notably Veit, believe that endometritis, pre-existing and aggravated by pregnancy, is the source of the reflex irritation. That this may be a factor in some cases is quite likely, but it can hardly explain the phenomena in most, or even in many, cases.

There are those who hold lacerations and erosions of the cervix responsible, but in most cases such lesions do not exist.

Coming now to the theory advanced and ably advocated by Dr. Graily Hewitt, I believe that we find here the chief, though not the only, cause. He is often quoted as teaching that anteflexion is the sole factor, but this interpretation is far from correct. He finds that "the alterations of the uterus proved by recorded cases to be most frequently present in cases of severe vomiting are:

"(*a*) Marked flexion forward and backward.

"(*b*) Rigidity of tissues of the cervix.

"(*c*) Impaction or detention of the uterus in the pelvis.

"These three factors are most frequently associated in various degrees of severity."

Upon these facts rests his theory that the reflex irritation consists in "undue pressure or tension of the nerve filaments distributed in the walls of the cervix, especially those in the vicinity of the internal os"; . . . "this pressure or tension may arise in any case in which that expansion process in the tissues of the cervix which is natural to pregnancy is delayed or obstructed by the condition of the cervix."

Now, if it be borne in mind that during the early weeks of pregnancy the uterus commonly gravitates toward the pelvic floor, it will at once be seen that any previously existing flexion must be exaggerated. If it be still further remembered that the normal condition of the uterus is one of moderate anteflexion, which our modern methods of dress, together with other injurious influences of civilization, too often make pathological anteflexion, the preponderance of cases of anteflexion in these statistics of vomiting of pregnancy will not be wondered at.

It will be noted, however, that flexion need not necessarily be present in order to explain the vomiting in accordance with this theory. If, by reason of a laceration of the cervix, with subinvolution and chronic metritis as a consequence, the tissues at and about the internal os have become so indurated as to prevent their normal and equable expansion, injurious tension of the nerve filaments is produced. If, again, the uterus be held down in the pelvis by firm adhesions, or by the added weight and bulk of a fibroid, impaction and injurious pressure are just as surely produced as in the case of a flexion. Other ingenious but less plausible theories have been advanced, but aside from admitting the general truth that almost any form of pelvic disease may in isolated and exceptional cases be a prominent factor, these theories need not be considered here.

My own belief is more liberal than is that of many who have written upon the subject, for while I hold most tenaciously to the general fact of a local cause to be found within the limits of the true pelvis, I yet admit most of the special theories above mentioned. Most prominently I should place Dr. Hewitt's explanation in its broadest interpretation, viz., anything that prevents the free and uniform expansion of the cervix, particularly in the immediate neighborhood of the internal os.

Following this are to be grouped indifferently the various factors of metritis, endometritis, lacerations and erosions of the cervix, and the sundry other forms of pelvic disease which may be operable in rare cases.

The above represented the best teaching of a dozen years ago, and it is as true to-day as when it was written; but careful observation and a considerable experience have in the mean time served to crystallize and confirm my beliefs. I find that in the vast majority of the cases anteflexion is present and the "impaction or detention of the uterus in the pelvis" is the result of contraction of the utero-sacra ligaments. Schultze has well described this contraction, due to parametritis posterior, which usually accompanies and aggravates anteflexion, but its influence upon the vomiting of pregnancy was, I believe, first pointed out by me some three years ago. I am convinced that in cases of this type, "the degree of the intractability of the vomiting and to a large extent the degree of its severity depend upon the degree of contraction in the utero-sacral ligaments."

Having now ascertained that, whatever the degree of pregnancy vomiting, it springs from some abnormal condition and not at all as a natural and inevitable result of pregnancy, we cannot escape the conclusion that there can be no such thing as "physiological" vomiting, and that, therefore, no difference save one of degree exists between the light and the severe cases. All vomiting during pregnancy, as at other times, is abnormal and must be so regarded and so treated.

Treatment.—It having been established that the chief factor in practically every case of vomiting of pregnancy is some abnormal condition of the pelvic organs, it follows naturally that the most effective treatment must be directed toward the removal or cure of such condition. And just here it should be urged that success in treating the vomiting will be in very close ratio to the accuracy of the diagnosis of the pelvic cause and the intelligence of the treatment applied to it. Let no one who has not good cause to consider himself competent correctly to map out the true condition of the pelvic organs rest content with the delusion that there is no pelvic cause for the vomiting because he can find none. In such a case no one but a well-trained gynæcologist is competent to pass final judgment, and it must be confessed that even he is fallible.

Most frequent in the list of abnormal pelvic conditions is anteflexion of the body or cervix, associated in most cases with more or less contraction of the utero-sacral ligaments. For this Graily Hewitt recommends gentle elevation of the base of the bladder and the superimposed fundus of the uterus with the finger. Failing thus he advocates the use of the air-ball pessary, which is to be inflated after insertion. This pessary must be perfectly spherical, and must, when distended, measure

not over two and one-quarter inches in diameter, the size rarely needing to be over two inches.

Aseptic precautions are to be observed before and after insertion, the patient to maintain the horizontal position, and the pessary to be removed at the end of six or eight hours. It may be necessary to repeat this treatment daily until the position of the uterus becomes permanently improved. Care must, of course, be exercised to prevent the induction of abortion by too great or too prolonged pressure due to the presence of the pessary.

Personally I have used this method but once, in which case it did good service. I have preferred to rely chiefly upon the frequent use of the knee-chest position, digital elevation, and packing.

In fact, so common is this condition as a factor, and so effective is the first part of the treatment alone, that I am in the habit of prescribing it as a routine treatment in the ordinary cases of pregnancy vomiting as they present themselves in the hospital clinics and in private practice, and I do not hesitate to assert that relief is complete in eighty per cent. of the cases.

The patient is told to assume a position on her knees, her hips high in air, her chest touching the bed, *every band being loose about the waist*, and then, either by opening the vagina with the finger or by introducing a glass tube, to admit air to the genital tract. This is done regularly night and morning, and at any other time when nausea is felt.

This failing, I place the patient in the knee-chest position and pack; lightly at first, but more firmly as she becomes accustomed to it. At first it is well to pack wholly in front of the cervix, so as to straighten out the flexion, but later a few tampons are best placed behind the cervix for the purpose of stretching the utero-sacral ligaments and so breaking up the impaction. Wool is the only proper material for this packing, as cotton soon becomes matted and hard; and the wool carded in sheets is far more elastic and therefore better than the fine tampon wool. The first one or two pieces may be dipped in a ten-per-cent. solution of ichthyol in glycerin, or in any bland antiseptic solution. I am in the habit of having all the tampons tied in a continuous string, like a kite-tail, so that the patient may be able to remove them at the first sign of irritation, or in order to use a cleansing douche before the next visit.

In one of these ways most cases of pregnancy vomiting may be relieved, but there remain those cases in which other causes are operative.

Retroversion and retroflexion are to be corrected by the aid of the knee-chest position, bimanual manipulation, and packing placed as high up as possible *behind* the cervix and extending down to the perineum. Once replaced the uterus is to be retained by some form of pessary.

In cases presenting erosion of the cervix, and in not a few cases showing no such sign, relief has promptly followed the nitrate-of-silver treatment. Indeed, so successful has this treatment proved in some hands that it has long been a routine method in the Vienna clinics. It is applied as follows: The cervix is exposed by a cylindrical glass speculum, the end of which it just fills, and after a thorough cleansing enough ten-per-cent. solution of silver nitrate is poured in to cover the exposed surface. After ten minutes this is decanted and the mucous membrane is dried. A second, and even a third, application may be called for after an interval of two or three days.

Should inflammatory processes be present, either in or about the uterus, the ordinary measures of rest, hot douches, and vaginal medication are in order. It is probably in such cases that benefit is had from vaginal suppositories or dressings of belladonna, cocaine, and morphine.

In all the more serious forms of the complication absolute rest in bed, in the horizontal position, is of much importance. Besides its general therapeutic value it permits the uterus more easily to rise above the brim, and aids us in our endeavors to correct displacements and lesser impaction. Coitus, and whatever may tend to cause sexual excitement or otherwise to increase pelvic congestion, must be avoided.

First discovered accidentally, and then practised empirically, Copeman's procedure has an established place in the treatment of severe cases. This consists in the careful dilatation of the cervical canal up to, but not through, the internal os. The index finger is used by preference, though Wylie has used a steel-branched dilator. Whether this acts by separating constricting bands of tissue, by straightening flexion, by breaking up impaction, or by some less apparent means, is not as yet agreed, but in many cases in which abortion has not resulted, a cure has been obtained.

Personally I wholly disapprove of this treatment, believing it to be dangerous and irrational. The same object is much better attained by the methods already described.

Besides the local cause, however, it is usually desirable to treat the conducting apparatus by which the reflex stimulus is conveyed. In other words, it is well to endeavor to lessen susceptibility to reflex irritation by the use of nerve sedatives, such as bromide, valerian, chloral, and even morphine. Chloral in full dose by rectum, night and morning, sometimes gives great relief, as does also morphine, introduced hypodermically or placed dry upon the tongue.

Chapman's ice bag to the spine has occasionally been found of service.

Then comes the long list of drugs for lessening the real or fancied irritability of the stomach. These must always be of secondary importance, and yet where symptoms are trivial they may answer every purpose at a minimum of annoyance to the patient, and where the outlook is grave we cannot afford to lose any help, however trifling, which may tend toward a cure. While, then, such remedies may always be given a place, reliance should not be bestowed upon them to the extent of wasting valuable time, or to the neglect of more rational measures.

In not a few cases gastric catarrh plays a more or less important part and claims attention. The ordinary remedies may be used, particularly the alkaline salines, taken well diluted before rising. Cocaine in small doses frequently repeated; creosote, or creosote and compound tincture of iodine in equal parts, given in one-drop doses every half-hour; oxalate of cerium in five-grain doses alone or combined with bismuth; calomel and ipecac in minute doses; hydrocyanic acid; tincture of nux vomica; pepsin; ingluvin; champagne; hot water; ice—these and other empirical means may be employed for their direct effect upon the stomach. In recent years the washing out of the stomach has been tried with manifest relief in not a few cases.

The diet and the mental surroundings of the patient must be carefully guarded. Our endeavor must be to keep up the strength at the same time that we spare the stomach needless effort by giving the lightest and most digestible foods. These are best given in small and frequent portions, it being borne in mind that often food will be retained if given just after a paroxysm of vomiting has spent itself. It must be remembered also that a patient can sometimes retain and assimilate an article of food for which she experiences a marked longing, when seemingly more appropriate articles are at once rejected. The simple expedient of giving a light and easily digestible breakfast an hour before rising will sometimes solve the problem in those ordinary cases which are known as "morning sickness."

When, however, the stomach rebels to such an extent that the patient's strength perceptibly fails, resource must at once be had to rectal alimentation. Peptonized milk, eggs, and predigested beef form the best basis for these enemata, to which may be added, if necessary, a few drops of laudanum and half an ounce of whiskey. Four injections, of four ounces each, given within twenty-four hours, can generally be retained, provided that once daily the lower bowel be well emptied by a

cleansing enema of warm suds. Life can be sustained for weeks in this way when all else fails.

Recognizing the fact that mental conditions play an important part in some cases, the patient must be cheered and encouraged at all times, and so far as possible all causes of worry, anxiety, and undue care must be removed.

We now come to that class of cases which resists all the measures at our command. The patient has reached the second stage described above, and the question of emptying the uterus presents itself. Of course it is assumed that no one will lightly decide upon this last resort without good and sufficient cause; yet, on the other hand, there is need to urge the danger of too long delay. Provided a faithful trial has been made of less radical measures, and yet in spite of them the gravity of the symptoms continues, let no time be lost in producing abortion, preferably by emptying the uterus at one sitting, under ether. The reason for thus urging against delay lies in the fact that even abortion may fail to avert the fatal issue if the third stage be permitted first to make its appearance. *Rufus J. Kingman.*

VULVA, DISEASES OF. See *Vagina, Diseases of.*

WACONDA SPRING.—Mitchell County, Kansas.

Post-Office.—Cawker City. Hotel and sanitarium

Access.—Trains on the Central Branch of the Missouri Pacific Railroad stop within a few rods of the hotel.

This big spring is located within a fine curve of the Solomon River, about three miles from Cawker City, and at an elevation of about 3,500 feet above the level of the sea. The spring is contained in the centre of a huge, circular mound composed of hard rock, which rises to a height of thirty feet above the surrounding surface. The spring is sixty feet in diameter, and is surrounded by a natural platform of rock from eighty to one hundred and fifty feet wide, and so nearly circular as to appear as if artificially cut. The diameter of the base of the mound is one hundred and seventeen yards from north to south and one hundred and nineteen yards from east to west, while its circumference is sixty-six rods. A stone coping has been placed around the spring, and this is surmounted by a light iron fence, to protect the water. Within ten rods of the spring a substantial hotel and sanitarium, supplied with all modern comforts and conveniences, has recently been erected. The water from the spring is supplied to this building and is utilized for the bath-houses, where all varieties of hot and cold or vapor baths will be found. The surroundings of this resort are very attractive, and the climate is of a bracing and salubrious character. The following analysis of the water was made by Prof. G. E. Patrick, of the University of Kansas, at Lawrence:

One United States gallon contains (solids): Sodium chloride, gr. 765.76; sodium bromide, gr. 0.23; sodium sulphate, gr. 183.60; magnesium sulphate, gr. 85.28; sodium bicarbonate, gr. 26.92; magnesium bicarbonate, gr. 27.56; calcium bicarbonate, gr. 31.30; silicic acid and nitrous acid, traces; no organic matter. Total, 1,120.65 grains. Carbonic-acid gas, 91 cubic inches to the gallon; specific gravity, 1.017.

The water has a strong saline taste, and when properly carbonated is clear and sparkling. The analysis shows a water of great potency. It should be fully possessed of the qualities found in the waters of this class. Taken in proper doses it is said to stimulate the appetite, to tone up the nervous system, and to invigorate the spirits and general bodily condition to a remarkable degree. It may be safely recommended in all cases in which this class of waters has been found useful. It is bottled and shipped to any desired point. *James K. Crook.*

WAHOO.—(*Euonymus*, U. S. P.; Spindle tree, Burning bush, etc.) The dried bark of the root of *Euonymus atropurpureus* Jacq. (fam. *Celastraceæ*).

This plant is a graceful shrub or small tree of the Middle and Western States, and is frequently cultivated for its beauty. It is usually about eight to twelve feet high, with opposite, oval-oblong, pointed, serrate leaves, and small, regular, dark purple flowers in axillary cymes. Sepals, petals, and stamens usually four; the latter inserted on a disc which extends over the ovary; pistil one; ovary three- to five-lobed and three- to five-celled, with several ovules in each cell; pods deeply lobed, smooth, bright crimson, drooping on long slender peduncles.

The bark occurs in quilled strips or pieces of very irregular size, usually with a few fine hair-like roots adhering; bark 1–5 mm. ($\frac{1}{25}$—$\frac{1}{6}$ in.) thick; outer surface ashy or pale brownish-gray, usually with some small dark patches, shallowly fissured and ridged, with a somewhat scaly and soft, friable cork; inner surface whitish or slightly tawny, indistinctly short striate; fracture short, whitish, or the inner layer pale-brownish in bark which has been long kept; when it is slowly broken, the fractured ends are held together by fine, somewhat elastic fibres; odor distinct and characteristic, more or less saponaceous; somewhat gummy in the mouth, the taste sweetish, bitter, slightly acrid.

The stem bark, which is in long, tough strips, with a dark gray or blackish cork, should be rejected.

The constituents of wahoo are not very well made out. Several resins, oil, wax, and numerous more ordinary substances have been obtained from it, as well as a glucoside named *euonymin;* indeed, several "euonymins," of somewhat different characters, have been separated by as many chemists. From all of these, again, is to be distinguished the resinoid "euonymin" obtained by precipitating the tincture. Of the latter there are two forms: the "brown," made from the official bark, and the green, made from the stem bark, the latter being inferior.

Uses.—Wahoo is a not very certain, usually gentle, but sometimes griping laxative, with a reputation as a cholagogue. It may be given in chronic constipation, or perhaps better in occasional attacks of constipation with dyspepsia, heaviness, and symptoms of diminished hepatic action.

Dose of the extract (*Extractum Euonymi*, U. S. P.), 1 or 2 dgm. (gr. i. ad iij.) in pill form once or twice a day. *Henry H. Rusby.*

WALLERIAN DEGENERATION.—The degeneration which occurs in the peripheral portion of a severed nerve fibre is known as the Wallerian degeneration. It is due to the separation of this portion of the fibre from its corresponding ganglion cell, and is usually explained as resulting from a loss of trophic influences, the severed portion being cut off from the source of its nutrition. The fact that a nerve when separated from its trophic centre degenerates in the direction in which it normally carries impulses is known as the *Wallerian law of degeneration.* It is also true that the central portion of a severed nerve —that portion which retains its connection with the ganglion cells—undergoes retrograde changes; but these differ from the changes seen in the Wallerian degeneration, being more of the nature of a simple atrophy.

The first recognizable change in Wallerian degeneration is a loss of the translucency of the nerve fibre. This is followed by a breaking-up of the myelin. Under the microscope the medullary substance is seen to be fragmented into small lumps or segments which become separated from each other. This is followed by a complete degeneration of the medullary sheath in which the latter is distintegrated into small fat droplets, the process suggesting an emulsification. At the same time there is a great increase in the size and number of the nuclei of the sheath of Schwann. Formerly it was believed that the neuraxones degenerated secondarily to the changes in the medullary sheath; but it has been shown that the changes in the former occur coincidently with those of the sheath. The neurilemma finally becomes filled with the remains of the axis cylinder and medullary sheath, the fat droplets are taken up by fat granule cells, and the detritus is in time absorbed by the cells of the neurilemma. In the neighborhood of the injury the nerve nuclei become en-

larged and show signs of proliferation. The neurilemma eventually disappears, but if the severed ends are again brought together, or if the distance between the ends is not too great, the old neurilemma sheaths may again become neurotized by new axis cylinders growing downward from the central cut end.

Aldred Scott Warthin.

WALLEY'S HOT SPRINGS.—Douglas County, Nevada.

Post-Office.—Genoa. Hotel.

This resort, formerly known as Genoa Hot Springs, is located about fourteen miles from Carson City, the capital of the State. The situation is picturesque, having an altitude of about four thousand feet, with high mountains on the west and a beautiful valley on the east. The prevailing weather is clear and pleasant, the temperature seldom exceeding 90° F. in summer or falling below zero in winter. Mr. H. J. Walley furnishes us with the following analysis made by J. W. Phillips, analytical chemist at the Nevada Agricultural Experimental Station: One United States gallon contains (solids): Potassium sulphate, gr. 0.67; sodium sulphate, gr. 12.41; calcium sulphate, gr. 2.19; sodium hyposulphite, gr. 0.40; sodium bicarbonate, gr. 0.64; sodium biborate, gr. 1.45; sodium chloride, gr. 4.78; silica, gr. 2.85; alumina, gr. 0.02; and traces of iron sulphate, magnesium bicarbonate, ammonia, and organic matter. Total, 25.41 grains. Carbonic acid gas, 6.48 cubic inches.

The temperature of the several springs (six in number) varies from 136° F. to 160° F. The baths here are stated to be very efficacious in the treatment of renal and skin diseases and in rheumatism of long standing. The analysis shows a valuable thermal water of the saline class.

James K. Crook.

WART. See *Verruca.*

WASATKA MINERAL SPRING.—Salt Lake County, Utah.

This spring is located in the northern outskirts of Salt Lake City. "Wasatka," or the "Milk Spring," derives its name from the peculiar soft and milk-like flavor of the water. During the past three or four years this water has come into extensive use, and it is said to give ample evidence of remedial value, besides furnishing an excellent table beverage. The following is a recent analysis by Walter S. Haines, professor of chemistry at the Rush Medical College of Chicago:

One United States gallon contains (solids): Sodium chloride, gr. 230.88; potassium chloride, gr. 3.06; magnesium chloride, gr. 21.24; calcium chloride, gr. 11.92; lithium chloride, gr. 0.12; ammonium chloride, gr. 0.25; calcium sulphate, gr. 59.50; calcium carbonate, gr. 4.75; silica, gr. 0.75; iron and aluminum oxide, gr. 0.03; sodium borate and magnesium bromide, traces. Total, 332.50 grains.

The water possesses alterative, aperient, and diuretic properties, and is recommended by Utah physicians in functional diseases of the digestive organs, liver, and kidneys. It is bottled and shipped to many points in Utah and the adjoining States. *James K. Crook.*

WASHINGTON, D. C.—Washington city (latitude 35° 53′ 39″ north, longitude 77° 2′ 48″ west), the capital of the United States of America, is in the District of Columbia, on the east bank of the Potomac River, about one hundred miles from its mouth. The Anacostia River (or Eastern Branch as it is sometimes called), a small tributary of the Potomac, bounds the city on the south, separating it and the suburb, Anacostia. Rock Creek, another small stream, which flows through the western part of the city, was at one time the boundary between the cities of Washington and Georgetown, but this municipal distinction is now not made. Between these two streams is an area of about eight square miles, having a general altitude of twenty to eighty feet above the level of the Potomac River. Upon this area the greater part of the city is built. Elsewhere the land rises to a general plateau, averaging from two hundred to three hundred feet above the river level, which also is practically sea-level.

The District of Columbia, originally styled "Federal Territory," was laid out in 1791 by commissioners appointed by President Washington, and in pursuance of an act of Congress, which gave the President the authority to select the site of the national capital. At the time of the selection, the District of Columbia was about the centre, geographically, of the original thirteen States of the Union. The original territory had an area of one hundred square miles, and was ceded, as equally as the nature of the site chosen admitted of, by the States of Maryland and Virginia. Subsequently, in 1846, the part given by the State of Virginia was ceded back to it by the national Government. The present area of the District is sixty-four square miles.

Washington has had no corporate existence apart from the District of Columbia since 1874. From 1802 to 1871 there was a municipal form of government, the chief executive being a mayor elected by the citizens. From 1871–74 the District and the city had a territorial form of government, the chief executive being a governor. Since 1874 the city and District have been governed by three commissioners, the Board of Commissioners of the District of Columbia, appointed by the President of the United States and confirmed by the United States Senate. These officials are appointed for terms of three years: two must be residents of the District for three years before appointment and of opposite political parties; the third must be an officer of the engineers, United States army, of a rank not lower than that of captain, and he must have served at least fifteen years in that branch of the military service. The Congress of the United States legislates directly for the District, and the commissioners execute the laws so enacted. There is thus in the capital of the greatest republic of history the spectacle of the citizens of that capital without direct representation in their own government. On the whole, however, the plan works well.

The population of the District of Columbia, according to the census of 1900, was 278,718, of which 191,532 were whites, 86,702 negroes or of negro descent, 455 Chinese, and 29 of all other races. Within what was the city of Washington as defined by its limits of 1874, there were 218,196 inhabitants, in what was Georgetown, 14,973, and scattered throughout the remainder of the District 45,973 inhabitants, mostly located in the suburbs known as Anacostia, Brightwood, Brookland, and Tenleytown. The average death rate of the District, including the city of Washington, for the last ten years is 17.57 per 1,000 for whites and 30 per 1,000 for negroes. The chief cause of mortality is tuberculosis. While there appears no undue prominence of any cause, contrasted with neighboring cities, there are certain conditions which, if removed, would greatly increase the longevity of the community. Typhoid fever has now a larger death rate than it will have when the contemplated water-filtration plant is in operation. Much improvement can be made in the sanitary requirements of house construction, especially in the matter of requiring ample initial air space in all dwellings, and in the prevention of overcrowding, particularly in the houses perniciously tolerated and still permitted to be erected in alleys and courts.

The water supply of the city is taken from the Potomac River about eighteen miles above the city, and is conveyed in a covered conduit to the distributing reservoirs. This conduit crosses a deep ravine on the famous cabin John Bridge, the largest single span stone arch in the world, two hundred and twenty feet from pier to pier, fifty-seven feet rise, and twenty feet wide. The distributing reservoirs being at a higher level than the greater part of the city, gravity is sufficient for household supply. However, there are several pumping stations for such parts of the city as cannot be fed by gravity. The quality of the water is soft, and during dry weather the water is clear. The water shed is not thick-

ly populated, there being no cities of any size within the area. So far, there has been no serious suspicion of typhoid or other infection emanating from the city water supply. From the frequency of rains, and the consequent turbidity, many persons object to using the city water on æsthetic grounds, and they resort to pumps within and to springs outside the city. There is reason to believe, from investigations made some years ago by the Medical Society of the District of Columbia, that these waters are more dangerous than the less inviting Potomac water. Contracts have been awarded for gravity sand filter beds, and when these are constructed and in operation the city will have a water supply of unimpeachable purity.

Sewage, both house and street, is removed by water carriage. At present there are several mains discharging at different points. Plans are in progress to converge these mains to a central pumping station, from which a trunk sewer will convey the total sewage across Anacostia River and thence along the Potomac, to be discharged into that stream some miles below the city.

The streets are wide, varying from sixty to one hundred and twenty feet, and are paved, with few exceptions, with asphalt. The street plan is simple. The original topographic map was designed by a French engineer officer, Major L'Enfant, into whose hands the work was entrusted by President Washington. The centre of the plan is the Capitol. Radiating from the Capitol are three streets, one running north, called North Capitol Street, one running east, East Capitol Street, and one running south, South Capitol Street. West of the Capitol a line of parks extends to the Potomac River. These streets and the line of parks serve to divide the city into four sections, denominated the Northeast, the Southeast, the Southwest, and the Northwest, respectively. What are distinctively named *streets* run east and west, and north and south, intersecting each other at right angles; another class, called *avenues*, intersect the streets and each other obliquely.

The east and west streets on each side of East Capitol Street and its westward park prolongation are designated by the letters of the alphabet (except that there are no J and X streets), and the north and south streets on each side of North and South Capitol streets are designated by numbers. The avenues are named after the different States of the Union. Streets and avenues receive in addition the names of the sections in which they are located. The city, however, has extended northward beyond the original street plan, and, as no provision had been made for uniformity in naming the new east and west streets, considerable confusion has resulted. Efforts are now making to rectify the oversight. The intersections of the avenues and the streets afford many opportunities for small parks, laid out in triangles, circles, and small rectangles. There are a number of large parks; the total parking area being somewhat over three thousand acres. A conspicuous feature of Washington is the great number of trees ornamenting the streets, and so thick are they that their summer foliage shuts out the houses from view.

As might naturally be expected the city has many public buildings. The most imposing are the Capitol, the Library of Congress, the Treasury, the State, War and Navy building, the Interior Department, the President's House (or popularly the White House), and the Post-office. The many other public buildings are not architecturally striking enough to be named.

The Capitol, the largest and most noticeable structure, has a length of 751 feet 4 inches, and a breadth varying from 121 to 350 feet, and covers an area of 153,112 square feet. The central part of the building is surmounted by an iron dome, 135 feet 5 inches in diameter at its base; on its top is Crawford's bronze statue of liberty, 19½ feet high, its crest towering 287 feet 5 inches above the earth. The body of the central part of the Capitol is built of freestone, the two wings of marble, and the dome, as above stated, of iron. The corner-stone was laid September 18th, 1793, by President Washington. The interior of the original building, at that time only the wings, was burned by the British in 1814. The present central structure was begun in 1818. The building as it exists at present was practically completed in 1865. The total cost has been somewhat in excess of $15,000,000. The Library of Congress, just east of the Capitol, is one of the most imposing structures to be found anywhere. It is built of granite, covers about three and three-quarter acres of ground, and cost $6,347,000.

Perhaps the most striking structure after the Capitol is the Monument, situated about a mile and a quarter west of the Capitol. This is a plain, rectangular, marble shaft, five hundred and fifty-five feet five and one-half inches high, and is the highest stone structure in the world. Its interior is hollow and is provided with a stairway and an elevator, both leading to a chamber just under the capstone. An excellent view of the city and surrounding country can be had from this point. Many small monuments and statues ornament the different parks. Educational advantages are excellent. There are ample public schools and the system of instruction is good. The Columbian University and the Georgetown University are old institutions, and offer first-class facilities for advanced instruction in all branches of study. The Catholic University of America, a comparatively new school, offers at present chiefly advanced instruction in theology and philosophy. The American University, a Methodist institution, is yet to be developed, but it promises to become a factor of educational importance. There are many smaller colleges and universities so called. The scientific work carried on in the different departments of the national Government gives exceptional opportunities for post-graduate work. The immense libraries—the library of Congress, that of the Surgeon-General's office, United States army, and of the other departments and bureaus of the Government—afford better facilities for gaining access to the literature of science than are to be found anywhere else in this country. There are a number of large and well-appointed hospitals. From a political and from a social view-point the advantages offered by the city, being the seat of the National Government, are obvious.

The facilities for living compare favorably with the other large cities of the country. The markets are well supplied the year round and prices are reasonable.

The climate is variable, but on the whole pleasant. A better idea can be had of it by consulting the table contained in the article on *Climate* in Vol. III.

W. F. R. Phillips.

WASHINGTON SPRINGS.—Washington County, Virginia.

Post-Office.—Glade Springs. Hotel and cottages.

Access.—Viâ Norfolk and Western Railroad to Glade Springs depot; thence two miles by hack or carriage to springs.

This resort is ensconced in a delightful location among the hills, at an altitude of 2,250 feet above the sea-level. The situation is opposite to and faces the White Top Mountain, one of the highest peaks in Virginia. Close by are the Chilhowee Sulphur Springs, Seven Springs, and Emory and Henry College. An excellent hotel, with provision in various ways for the comfort and amusement of the guests, is maintained. The springs are seven in number, and have an average flow of thirty gallons per hour. The water has a temperature of 51° F. We present analyses of the "Sulphur" Spring and the "Magnesia Soda-Iron" Spring, by W. H. Seamon, analyst of Crozet, Va.:

One United States gallon of the "Sulphur Spring" contains (solids): Iron carbonate, gr. 0.52; calcium carbonate, gr. 2.99; potassium carbonate, gr. 0.11; sodium carbonate, gr. 0.29; calcium sulphate, gr. 6.47; calcium phosphate, gr. 0.14; sodium chloride, gr. 0.09; strontium sulphate and arsenic chloride, traces. Total, 10.41 grains. The water also contains a certain amount of hydrogen sulphide.

One United States gallon of the Magnesia Soda-Iron Spring (Washington Spring) contains (solids): Calcium sulphate, gr. 0.10; magnesium sulphate, gr. 4.04; stron-

tium sulphate, gr. 0.38; sodium sulphate, gr. 3.97; iron carbonate, gr. 1.95; calcium carbonate, gr. 13.66; sodium chloride, gr. 0.34; potassium chloride, gr. 0.24; silica, gr. 2.07; organic matter, gr. 1.03; aluminum sulphate, manganesium carbonate, and phosphoric acid, traces. Total, 27.78 grains. These waters have a useful application in debilitated states, especially when attended by intestinal torpor. They have rendered good service in anæmia and general debility. *James K. Crook.*

WATER (H_2O).—Even after it had ceased to be considered elementary, there was much ignorance concerning the composition of water. Thus when for the first time it was decomposed by the action of the electric battery, an acid was observed to form at one pole and an alkali at the other, in addition to the gaseous products oxygen and hydrogen. This acid and the associated alkali were supposed to be intimately related with the two gases in the structure of water, until Humphry Davy, by a series of brilliant experiments, showed that the acid and alkali were entirely adventitious and that water consisted of oxygen and hydrogen alone. Demonstration of its composition was also made synthetically by the explosion of a mixture of the two gases, such mixture being in the ratio of one volume of oxygen to two volumes of hydrogen.

Considered physically, an important property of water is its very great solvent power, and it is also noteworthy as the basis for specific gravity and specific heat. Moreover, it is employed as the metric unit of weight, the "gram" being the weight of 1 c.c. of water at the temperature of its greatest density, 39.2° F.

Chemically considered, the graphic formula for water, H—O—H, known as the "water type," constitutes the starting-point of the two great series of compounds known as "hydrates" and "oxides," the first being formed by the replacement of half the hydrogen of the "water type" by a metal (R—O—H), and the latter by its entire replacement (R—O—R). For our present purposes, however, it is the more practical and sanitary side of the question of "water" that should claim our attention; in other words, we should undertake some consideration of the wide field of inquiry covering *water supply*.

From remote antiquity the highest value has been set upon an abundant and pure water supply. Centres of population sprang up in ancient times around those points where it was readily available, and great expenditures of labor and treasure were made to carry it to places where it was not naturally plenty. Not only was a generous daily *per capita* allowance sought for, but we note in the centuries gone by unmistakable evidences of a keen appreciation of the dangers lurking in a polluted supply; and upon this point many of the ignorant consumers of our own day and generation would be benefited did they consult the wisdom of the past.

When considering the sources of water supply available for public or private use, we very properly first turn to such bodies of "stored water" as may be within reachable distances.

Nature provides enormous quantities of water stored up in lakes and ponds ready for human consumption, and man frequently supplements this by impounding surface and deep-seated waters in artificial basins when the natural reservoirs of the district are unavailable or are insufficient in size.

Lakes of such magnitude as to be properly considered inland seas—the Great Lakes of North America, for instance—furnish water of quite constant composition, free from the considerable vegetable contamination so frequently met with in small lakes and ponds.

Large as these Great Lakes are, the influence of the sewage from cities upon their shores is nevertheless beginning to be seriously felt. For instance, the pollution of Lake Michigan by the sewage of Chicago is a widely known fact, and the intakes, situated as they are miles from shore, are frequently reached by the ever-swelling volume of the city's refuse.

	Lake Superior, near Duluth, 40 miles out from shore, March, 1896.	Lake Erie, near Erie, Pa., 14 miles out from shore, October, 1897.
Free ammonia	0.03	0.045
Albuminoid ammonia	.02	.112
Chlorine	1.0	3.500
Nitrogen as nitrates	0.0	.080
Nitrogen as nitrites	0.0	Trace.
Required oxygen	1.15	1.250
Total solids	54.0	134.000

Much opportunity is given in large lakes for sedimentation to come into full play, and settlement is, in consequence, a very great item in the process of the natural purification of their waters; but so far as the American "Great Lakes" are concerned, a difference must be noted in this respect between Lake Erie and the other members of the group. Lake Erie is comparatively shallow and is stirred to its bottom by every gale. Therefore sedimentation advantages are at a minimum therein.

In small lakes and storage reservoirs vertical circulation commonly ceases below a depth of twenty feet, that being the usual distance to which wind and wave agitation extends. Fitzgerald found that Lake Cochituate, which has an area of seven hundred and eighty-five acres, is not affected by wind and wave action below twelve feet from the surface. Should a lake be protected from the wind, the aerated layer may extend temporarily only ten feet from the surface, and below this level the cold, stagnant water rests, until such time as the chilling of the upper layer increases its gravity to and beyond that of the lower layer upon which it floats. When this point is reached, readjustment of relative position is immediately instituted, in accordance with the change in specific gravity, and the water of the lake "turns over."

The formation of this stagnant layer begins in April in this latitude, and circulation is partly re-established in October and completely so in November. With the advent of freezing weather a second period of stratification is inaugurated, which continues until the surface thaws again in the spring. Vertical circulation then progresses until the warm sun of later April renders the surface water so light as to float upon the colder layers beneath, when summer stagnation again begins.

Whenever the lower stagnant layer is brought in contact with decomposing organic matter, as is the case in reservoirs with bottoms from which the vegetation has not been removed, the dissolved oxygen present is quickly used up; quantities of extractive matters pass into solution and the water becomes foul in odor and dark in color.

Even though the bottom of a lake or reservoir be perfectly clean and sandy, the dissolved oxygen must surely diminish in the lower layers of water, for no water is without some oxidizable contents, but it will not be reduced to zero, nor will the water become damaged in quality.

Uniform experience goes to prove that good water may be preserved in properly constructed reservoirs without deterioration for indefinite lengths of time. It must be remembered, however, in this connection, that to keep a ground water in good condition it is necessary to cover the reservoir. Such waters are usually charged with mineral matter suitable for plant food, and the higher organisms will be very likely to grow therein unless light be excluded. Reservoirs used for storing filtered surface waters should be likewise dark, for the same reason.

Algæ depend for their development upon material furnishing nitrogen. Water containing a moderate amount of this element washed from natural sources will maintain but a small growth of such plant life, but where nitrogen is present in great quantity as nitrates, as is frequently the case in deep-seated waters, the development of algæ is often excessive during reservoir storage,

and the resulting smell and taste given to the water may cause widespread complaints.

It is true that no relation has ever been established between the occurrence of disease and the presence of the bad tastes and smells occasioned by abundant growth of algæ, but the results directly traceable to such growths will not be tolerated by the public, and the water purveyor constantly finds himself much more open to criticism through difficulties of that kind than through pollution of the supply by drainage from pathogenic sources.

Properly to conserve a water, to put it tersely, it may be said that if it be from a dark source it should be stored in the dark, and *vice versa;* filtered water being the exception, and requiring dark storage irrespective of its source.

If dark storage be not practicable, then a water from an underground source should be delivered for use at the earliest moment possible to avoid the growths which the presence of light will encourage. With surface waters, on the other hand, open storage is always of benefit if the reservoir be clean.

It is an error to suppose that "stagnation" in a properly prepared reservoir is of itself harmful to the quality of water. Quite the contrary is true, and it is scarcely too much to say that rest rather than motion is the condition commonly leading toward the greatest amount of "self-purification."

Pathogenic bacteria tend to diminish by storage, both by reason of settlement and because of conditions which are adverse to their requirements for life; hence we note the beneficial value of the time element when dealing with impounded waters. Running streams, on the other hand, lessen the opportunities for sedimentation and their rapid flow hastens the delivery of the yet living disease germs to the unsuspecting consumer.

Let it not be thought, however, that the popular belief in the purification value of thorough aeration is based entirely upon error. Gases dissolved in the water and giving it objectionable odor—as the sulphureted hydrogen, for instance, in the artesian supply of northern Florida—are driven out by thorough exposure to air; and even algæ growths are often impeded by vigorous agitation. To such extent, therefore, falls and rapids and reservoir fountains are of advantage for the improvement of water; but the really serious item of pollution, namely, sewage admixture, cannot be disposed of by so simple a method as direct atmospheric oxidation, and any hopes that are based upon the supposed efficiency of such action will be doomed to disappointment.

A very large number of cities derive their water supplies from purely surface sources, such as rivers and streams—in Europe after careful filtration, but in America usually without such purification.

One of the important things for the consumer of such a water to bear in mind is that sudden and great changes in the character of the water are to be expected. Much will depend upon the weather and the amount of surface wash which naturally flows toward the drains of the district. A river which is clear to-day may be muddy and less fit for use to-morrow, and the turbidity will persist, even after its direct cause has ceased, until the river and its tributaries shall have emptied themselves into the sea. For it must be noted that the clearing of running streams has little to do with sedimentation and is almost wholly dependent upon a running out of the roily waters.

Another change, slow in operation but serious in results, is that induced by the establishment of sewerage systems in river towns, through the growth of a population which naturally sewers into the river. The difficulty is twofold. Not only does pollution increase with the multiplication of the people producing it, but the partial soil purification of the contents of the village cesspool is entirely eliminated when the sewers of the growing town turn the sewage in the raw state into the river.

It is not unusual to find a city damaging its own water supply by its sewage outflow. Tidal action may carry the refuse of a town up stream from the sewer outfalls until the water works intake is reached; or else the currents produced in a lake by weather changes may accomplish the same result, as is noticed at Chicago.

The self-purification of streams is a topic which has been very fruitful of discussion. Pettenkofer held that sewage might be safely turned into any stream whose volume was fifteen times greater than the volume of the sewage, and whose velocity was not less than that of the sewage inflow. This is but an *ex-cathedra* statement of a rather widely spread belief in the ability of running water to purify itself after a comparatively short flow. That efficient purification by such means is far from being an established fact is attested by the many instances that might be quoted of typhoid infection having been carried many miles from the point of pollution to the city intake below.

How far such infection may be carried is uncertain and is governed by the velocity of the current, but the distance has been shown to be many miles. The germs of such a disease as typhoid fever do not find conditions suitable for their development in river water, hence they do not multiply therein and after a time they die out without causing disturbance, provided that they be not caught up by some down-stream intake before their death be accomplished. Hence the value of the element of time in rendering a polluted water again fit for consumption. Not infrequently an acceptable water may be found flowing from a lake of no great size, while the stream tributary to its other end may be distinctly polluted; the lapse of time and the advantages of sedimentation having united their efforts toward the promotion of purity.

While space cannot be here given to detailed accounts of the ravages that have been caused by infected water, yet a glance at a single instance may serve for general illustration.

The cities of Hamburg, Altona, and Wandsbeck are practically one and are separated by only imaginary boundaries which a stranger could not locate. In 1892 Asiatic cholera broke out in Hamburg with exceeding severity, the reported cases having been 17,020 with a death list of 8,605. The disease marched up to the invisible boundary lines and there stopped, confining itself almost exclusively to Hamburg. In one street, which for a long way forms the boundary, there was cholera on the Hamburg side, whereas the Altona side was practically exempt. There was one detectable difference, and only one, between the conditions obtaining in these adjacent cities—they had different water services. Hamburg took raw water from the polluted Elbe River; Altona used the same river water, still more polluted by the Hamburg sewage, but carefully purified it by sand filtration; Wandsbeck possessed an entirely different supply. How cholera located the boundary is best shown by a "spot map" of the reported cases. (Fig. 5031.)

Freezing is a means of natural purification of water upon which the popular mind lays great stress, and to a certain extent the general confidence in its efficiency is not misplaced. Ice is certainly purer than the water from which it is formed, often very greatly purer. The ice cake grows from the surface downward, the crystals as they form pushing away from them the material suspended in the water, bacteria included, and freeing themselves also from no small amounts of even dissolved impurities. Naturally some floating objects become entangled in the thickening mass, particularly so if the underlying water be shallow, and all must of necessity pass into the ice cake if the entire depth of water be frozen. An excellent idea of the exclusive action of the crystals may be had by examining a cake of artificial ice. It will be observed that the last part frozen, namely, the centre of the cake, shows marked inferiority, due to the floating objects having been driven inward by the forming ice, only to be at last caught by the final solidification of the central portion.

When ice is formed on a polluted but deep water, a large river, for instance, the amount of bacterial purification amounts to over ninety per cent., commonly over ninety-five per cent., and a further element of

safety lies in the fact that storage in ice-houses during the months elapsing between the winter "harvest" and the summer distribution tends still further to reduce the number of germs present in the ice cake. Be that as it may, however, there is small excuse for the too common practice of cutting ice from grossly polluted waters, for with even a high percentage of exclusion some germs do enter the ice, and it has been shown that typhoid germs are at times capable of surviving a three months' imprisonment therein.

Touching upon this question of the ability of typhoid germs to withstand freezing, the instance of the epidemic at Plymouth, Pa., is a case in point. There the dejecta of a patient lay frozen upon a hillside from January until March, when they were washed by the melting snow into the city water system with most disastrous results.

Stress should be laid upon the fact that the large percentage of bacterial purification which results from freezing, as above referred to, is due to the mechanical exclusion of suspended particles by the growing crystals and not to a mere lowering of temperature. Even the intense cold of liquid air is but indifferently germicidal.

Beyond the ordinary wash caused by storms upon every water-shed, some rivers are exposed to sudden and great concentration of pollution through the sweeping away of piles of filth which accumulate upon their rocky fore-shores during periods of low water. The Tees, a river of northern England, is of such description. A study of the epidemic of typhoid which prevailed in that valley in 1891 proved of special interest, because the disease confined itself to those communities, aggregating 220,000 people, who used the river water, to the exclusion of a population of 280,000 of the same district who drank water from other sources.

A further point of interest lay in the striking manner in which a chart of the reported cases showed a rise in the number of fever patients about fourteen days after each heavy rainfall. (Fig. 5032.)

Streams in Europe are frequently polluted by the washing therein of infected linen, an out-of-doors laundry being common enough in the Old World, although quite the reverse in America. To such a cause was ascribed the great cholera outbreak at Messina in 1887, and a like epidemic at Cuneo in 1884 was traced to an entirely similar source.

"Deep-seated" is a term applied to water of a distant origin to distinguish it from "ground water" of an entirely local source.

Springs of small flow, such as trickle out of the country hillside, are properly classified with shallow wells; they furnish "ground water" only and are of local origin.

Quite another matter, however, are those natural fountains which reach the surface in great volume, possessed of a temperature radically different from that of the local subsoil, and holding in solution mineral materials that may be quite foreign to the neighborhood. Such water is always of distant source, and the gathering grounds where it originally falls as rain may be very far away indeed.

Picture the outcrop upon some rainy upland of a porous stratum, encased upon either side by strata impervious to water; let the strata be possessed of a moderate dip, then let them be cut transversely at some point below, either by simple erosion or by a geologic fault, and the conditions for a deep-seated spring would be complete. Rain water falling on the distant outcrop would pass down the porous stratum, picking up soluble material on the way, and would escape as a spring at the point where the strata were broken or eroded.

At the head of San Antonio River, not far from the city of San Antonio, Tex., is situated a mammoth spring of pure water, whose daily outflow is some fifty million gallons. This spring is but one of a group of great springs which "coincide almost exactly with the line of the great Austin Del Rio fault." A very curious instance of a spring of great magnitude caused by erosion cutting into the water-bearing stratum is to be found several miles out at sea off the coast of Florida, east of Matanzas Inlet.

There are reasons for believing that the Matanzas spring is due to a bursting of the confined waters through a hole in the upper hard rock layer. Successful sounding has recently been accomplished in the spring itself. In its immediate vicinity the ocean suddenly deepens from a depth of sixty to one of one hundred and twenty-six feet.

Instances are by no means rare of the use of deep springs for water supplies of magnitude, such as the "Vanne" water, which supplies a part of Paris from

FIG. 5031. Chart showing Distribution of Cholera Cases, in the Epidemic of 1892, at Hamburg and Altona. ——, Boundary between the two cities; • •, cases of cholera; ○ ○, cases imported from Hamburg.

springs in massive chalk near Troyes, but deep seated water is much more commonly reached by special borings.

The expression "artesian" has been extended to include deep wells under all conditions, but without proper

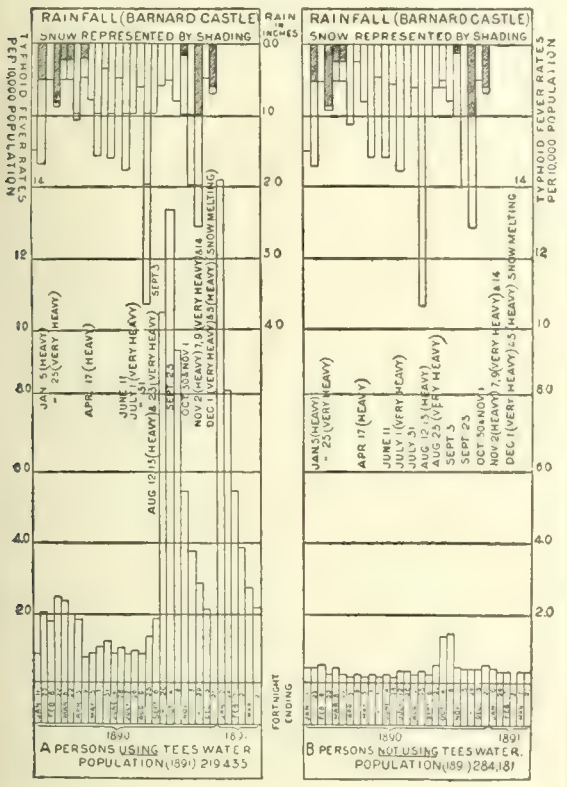

FIG. 5032.—Rainfall and Typhoid Fever in the Tees Valley, England.

license, because the term originally came from the name of the French province where deep wells were first successfully established, and such wells were "flowing." It is therefore to "flowing wells" only that the expression "artesian" properly attaches. Wells of this class were first sunk, in Europe, at Lillers, in Artois, in 1126. In the Sahara and in China they have been known for many centuries. Whether, however, the well be a flowing one or one from which the water has to be raised by power, the conditions governing the storage of such water are essentially the same as have been already given when speaking of deep springs. An outcrop of a porous stratum in a rainy upland acts as the collecting area; this stratum is of moderate dip and is enclosed by other strata, impervious to water, lying above and below.

Unless the strata form a basin or pocket, the water of the porous layer will find its natural outlet in a spring form where the layer is cut transversely by erosion or fault; but should a well be sunk at some intermediate point the water will rise in the same, or overflow, to a degree dependent upon the head to which it is subjected; that is, to the elevation of the gathering grounds above the well, and to the freedom with which the water can flow down the porous stratum and escape through the outlets below. (Figs. 5033 and 5034.)

It must be remembered in this connection that the expression "deep" refers to the non-local character of the water rather than to the depth of the hole required for tapping the same. In fact, "deep water" may lie very near the surface in some places.

Contrary to the belief of many people, deep-seated water is not inexhaustible. If the porous layers containing it be extensive, an immediately available supply of large volume, which is the accumulation perhaps of ages, may be counted upon; but should the daily drain be larger than the natural reinforcement, the delivery must surely shrink in quantity and finally cease.

It is common knowledge that a great volume of water, some sixty-six million United States gallons, is drawn daily by the London water companies from deep wells in the chalk.

The serious effect of extending and heavily pumping these deep chalk wells supplying a portion of London is that "for every two gallons of water collected within the Lee valley London is withdrawing three from its reservoir in that chalk basin, and this quite apart from the amount every day required by the resident population of that area. The result of such a process can only be a steady, if gradual, exhaustion of water from the chalk and a progressive lowering of its plane of saturation."

Water from deep sources has commonly characteristics of its own, distinguishing it from the ground water of the neighborhood. One of the most easily recognized of these is high temperature.

Another peculiarity of deep water is the small quantity of dissolved oxygen which it usually contains. This is by no means due to the pressure to which it may be subjected, for increase of pressure favors the solution of gases, but is rather owing to the abundant opportunity for removal of oxygen by contact with such substances as organic matter, and compounds of iron and manganese, presented during the long underground journey of the water from its place of collection.

In point of composition the waters of deep wells are almost always highly mineralized, as would be expected in consideration of the items of long time, long distance of flow, high pressure, and elevated temperature. Sometimes the materials contained render the water unfit for use, even for boiler purposes, but more commonly the supply is such as to be considered a great boon to the fortunate possessor.

Perhaps as noteworthy an instance of a flowing well as can be quoted is that of Woonsocket, South Dakota. The boring is of seven inches in diameter and seven hundred and fifty feet deep. The water is of 63° F. temperature and is thrown above the surface to a height of

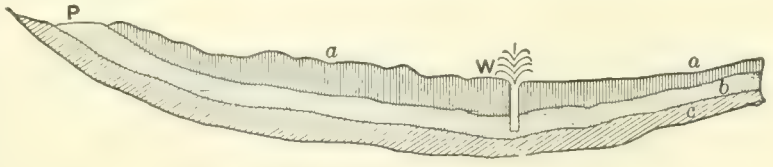

FIG. 5033.—Condition Favorable for Flowing Well. (After Hay.)

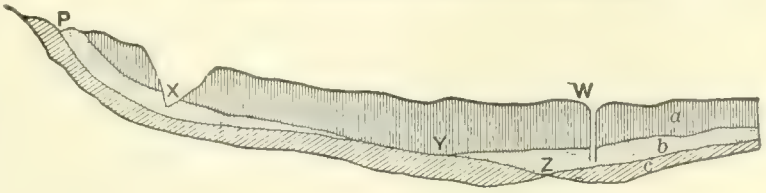

FIG. 5034.—Condition Unfavorable for Flowing Well. (After Hay.)

eighty feet in a magnificent fountain, the entire discharge amounting to 11,500,000 gallons per twenty-four hours. The well is capable of furnishing a pressure of one hundred and forty pounds per square inch.

The circulation of the "ground water" in the soil is

governed by gravity and surface tension, and the latter is in turn affected by the structure of the soil, its composition, and the per cent. by volume of the empty spaces between its particles.

The rate at which water will flow through a soil is dependent not only upon the aggregate volume of the voids, but also, and more particularly, upon their separate dimensions; for it can be readily seen that the inhibiting influence of friction will rapidly increase with the fineness of the soil grain.

Values are on record for the water-holding powers of various soils, but a word of caution seems proper here. It must be remembered that such figures show what the sands and soils will *hold*, not what they would *deliver*. No pump could extract that final portion of the contained water which would remain as "moisture," and its quantity would be a very respectable percentage indeed of the amounts given.

Wherever found, and under whatever circumstances, the water of the ground owes its origin to the rain or melting snow. Attention is called to this point because of a widespread notion that the wells of fresh water often existing in the immediate vicinity of the ocean are fed with sea water from which the salt has been removed by percolation through the sand of the beach. This inference is permitted in an engineering work of national fame. All along the shore of the Italian Riviera the traveller can see wells dug within one hundred and fifty feet of the surf. In such cases the fresh water found originates some considerable distance inland, and the wells intercept it on its way toward an outlet in the sea; in other instances its origin is due entirely to very local rains, and its storage in the loose sand is owing to its being specifically lighter than the surrounding sea water.

An instance of this kind is met with near the island of Heligoland. About a mile east of the island there is a long strip of sand raised but a few feet above the level of the ocean, extending some half a mile in length and but two hundred yards wide. It was formed and is maintained by ocean currents, and is covered by a scanty growth of grass. Anywhere upon this islet fresh water may be obtained by digging in the sand. Necessarily the water to be secured from such a source is limited in quantity.

A commonly received conception of the occurrence of ground water is that it moves in very definitely localized streams, and that, to be successful, a well must be sunk directly into one of these. Of course the conformation of the country may at times cause this popular notion closely to coincide with the truth, but a more general description of the occurrence of ground water would be that of a widely extended sheet, and the expression "water table" has been adopted with that view in mind.

The mean height of this "water table" (*i.e.*, its distance from the surface of the ground) is governed by the average rainfall and the opportunities for local drainage. The delivery being into the rivers and streams of the district, or into the sea, there is always a slight inclination of the water surface toward those natural drains, more especially in their immediate vicinity.

When the conditions prevailing in the district do not favor the development of a spring on the side or at the base of a slope, the time-honored manner of tapping the underground supply is to sink the ordinary domestic well into the water table.

For the delivery of large supplies the ground water cannot be conveniently tapped by ordinary dug wells, so that recourse is had in such cases to what is known as "driven wells," set within suitable distance of each other, and coupled to a general main through which the water is drawn by the pump.

Each well is but an iron tube, perforated at its lower extremity, which is driven through the soil to the water-bearing layer below. Single wells of this description, surmounted by a simple hand-pump, may be seen, in some instances, replacing the domestic well in the country dooryard, but the type is more commonly met with in "gangs" of very considerable number for the supply of cities or towns.

A method of sinking them by the use of live steam was patented a few years ago, and, under some conditions of soil, may show considerable saving in first cost.

By whatever method the "driven well" is sunk, its mode of action is entirely similar to that of the common domestic well, from which it differs only in diameter, and it is supplied by the ground water of the district in the same manner as its longer-known progenitor. There is, in short, nothing gained in the majority of cases from the supposed exhaustion of air by the action of the pump. Much has been claimed under this head, and it has been urged that the zone of influence always widens rapidly under "suction" from an air-tight well; but it must be remembered that "air-tight" is a term which can be usually applied to the well only, and not to the ground overlying the zone of influence. The porous soil will unquestionably admit all the atmosphere required, and consequently the flow of water will be determined by those forces, and those only, which govern in the case of wells of the ordinary type.

When, however, the well passes through an extensive layer of impervious clay, and taps a water-bearing stratum beneath, then the opportunities for a development of the advantages of "suction" reach their maximum.

A fact often lost sight of is that driven wells, so far as a permanent supply is concerned, are dependent upon the amounts of rainfall, "run-off," evaporation, and plant requirements. There is not, contrary to popular conception, an underground reservoir from which unlimited quantities of water may be pumped. It is true that a reserve storage exists, that may be drawn upon in time of drought, but nature keeps a strict account of such matters, and the deficiency created in time of need must be made up during the period of plenty; otherwise the delivery of the plant will gradually diminish and ultimately entirely cease.

One very material advantage possessed by a driven well over a dug one is that it can be sunk deeper in the water-bearing sands at small expense, and, with a long strainer, can take water throughout a great fraction of its length. A dug well, on the other hand, has its construction hampered after water is reached, and its cost per foot is greater beyond that point; so that it commonly has to depend principally upon its bottom for supply, tapping, as it does, only the upper portion of the ground-water layer.

Closely related to the well systems already spoken of, the "infiltration gallery" stands as a widely used method for securing the water of the ground. Such a gallery is really but a dug well with one very long horizontal axis. Its position is usually near, and parallel to, the banks of some stream, such a site being chosen with a view of securing its supply from the water of the river. Except under exceptional circumstances, however, the water reaching the gallery comes from the landward side, and is the ground water of the district for which the river is the drain.

Rivers may indeed diminish in volume as they flow onward, and may even entirely disappear by sinking into the ground, as is the case with a number of streams flowing down the slopes of the Rocky Mountains, but this condition is distinctly exceptional. A river is commonly to be regarded as a drain, into which water is received, but from which none flows.

Dependence is constantly laid upon the excellent filtering powers of these underground galleries, and they justify it during the earlier periods of their use, but, considered as a filter, such a device is beyond cleaning and repair; it may clog, or, on the other hand, ruinous channelways may follow heavy pumping. In the first instance no water, and in the second instance polluted water, may result.

The opportunity for the contamination of well water, particularly that of the common domestic well, is often very great. No proper conception of the right location for the house well ever seems to enter the minds of most

of our rural people, and if water can be had from a spot conveniently near for general housework, inquiry as to the quality of such supply is usually considered quite superfluous.

In some towns the local boards of health determine the minimum distance to be allowed between a well and an uncemented privy vault, and such distance is most commonly fixed at fifty feet. The permitted distance in at least one instance is twenty-five feet, and in another the minimum distance allowed is twenty feet!

That any such distance of soil filtration can protect a well from pollution, provided the polluting source be constant in character, is beyond even hoping for, and many instances could be given showing how even considerably greater distances have also failed.

Two causes for failure are, first, overtaxing the purifying powers of the intervening soil by presenting a constant flow of more polluting material than can be oxidized; and second, the opening up of cracks in the subsoil whereby direct connection with the well is assured.

The serious Maidstone epidemic of typhoid was due to the latter cause. An unusual drought had occurred, which caused deep cracks to open in the stiff soil, so deep that the health officer thrust his cane into some of them without finding bottom. Later there was a heavy fall of rain which washed surface filth carrying typhoid excreta into these fissures and produced a material rise in the ground water. Of course there was lack of efficient soil filtration.

It is a fatal error to fancy that because a water has a bright, sparkling, clear appearance and a pleasant taste, therefore such water is wholesome. Carbonic acid gas is what causes the brilliancy and refreshing taste of a ground water, and to the solvent action of that gas is due the clearness of many waters which nevertheless hold much organic matter in solution. When it is borne in mind that carbonic acid is one of the products of sewage decomposition, the inference as to its possible source in the case of some well waters is not a pleasant one.

It is often objected that certain well waters have been in use for many years without bad results following. Possibly; but it must be remembered that the imbibition of sewage derived from healthy sources may be quite harmless, unless it be in too concentrated a form, however undesirable it may be from an æsthetic standpoint. The serious part of it all is that the sewage which contaminates the well water may, during an epidemic, suddenly become pathogenic in character, and then the well becomes a distributing centre for disease. A city well is always to be suspected, and if, upon examination, its water is found impure, it should be forthwith ordered closed, particularly under circumstances such as threaten invasion of epidemic disease.

An excellent way to determine the probability of objectionable drainage material entering a well is to place a quantity of a solution of common salt, of lithium chloride, or of fluorescein at the point whence contamination is supposed to come. The normal composition of the water being known, there will appear an increase in "chlorides," a spectroscopic test for lithium, or a decided fluorescence in the water if there be drainage from the source in question.

Although of somewhat uncertain reliability as to quantity, rain water is universally looked upon with much favor because of its assumed excellence as to quality, and yet even a casual inspection will often show it to be a long way from pure, and it may possibly be polluted to an extent quite surprising to the collector of the supply.

The roof upon which rain is caught is a twofold cause of impurity in the collected water; first, because of the material of which the roof is constructed, and, second, because of the foreign substances that may settle thereupon.

In cities the amount of street dust blown upon the roof and afterward washed into the cistern is much greater than is commonly supposed. Soot, excrement of birds (often a large item), fallen leaves, and various mossy growths are among the sundry additions to be found in a roof-collected water.

It is exceedingly important that every cistern should be inspected and cleaned frequently, and upon no point does the public require more instruction than this.

While its softness recommends it for use in the laundry, and while the absence of lime salts renders it desirable for cooking, rain water is, on the whole, not to be considered so suitable as a pure ground or surface water for general domestic supply.

Ice, especially in America, is certainly to be reckoned as an article of food, and the prevalent belief that water purifies itself during the act of freezing is so well fixed in the public mind that the source whence ice is harvested is in consequence usually considered unimportant. This belief is not without support in fact, as we have seen, but, like many another partial truth, it is a very uncertain foundation upon which to erect the best form of sanitary procedure.

As has been already stated, we may depend upon the growing ice crystals mechanically excluding much of the germ life during the process of freezing, and such exclusion would appear to lie between ninety and ninety-five per cent. of all bacteria present in the water, or, more strictly speaking, the above percentages would represent the bacterial purification from all causes during freezing, of which causes mechanical exclusion is one.

Artificial Purification of Water.—Pure water is becoming more and more difficult for many of our towns to secure, so that the best that some of them can hope to obtain is a polluted water which has been efficiently purified by art. It is a question, sometimes, whether it would not be better policy, considering the rapid changes in the density of population, to accept a moderately polluted source and thoroughly purify its water, rather than go to large expense in obtaining a faultless supply which might have to be purified in its turn at some later day.

Further, it must be borne in mind that, outside of any question of wholesomeness, the water which a part of our people are content to use at present will not be considered suitable in a few years to come. The tendency is toward a general demand for a clear and colorless water, and water purveyors must be prepared to meet it.

Filtration of surface water, before delivering the same for public consumption, is now specifically ordered by the laws of Germany, and rules are laid down for its proper accomplishment. Such legislation is not improbable in this country, thus still further making it the part of wisdom to anticipate the artificial improvement of some waters which are now possibly considered beyond impeachment.

The method of purifying water on the large scale which deserves first attention on account of its early use and wide application is that of "slow sand filtration," commonly known also as

The English Filter-bed System.—Briefly described, an English filter bed is a tight reservoir, suitably underdrained, and containing some five or six feet of stratified filtering material, of progressive degrees of fineness, beginning at the bottom with broken stone or gravel, and ending with an upper layer of fine sand. Through the fine-sand layer the water slowly and evenly passes, leaving the bulk of its suspended impurities upon the surface to form the *Schmutzdecke*, or "dirt cover," of the Germans.

Beyond the mere gradual accumulation of suspended matter strained from the water, this *Schmutzdecke* is in part composed of slimy, jelly-like material, produced through bacterial agency, which serves to entangle and hold bacteria and other suspended substances of all kinds.

It must not be thought, however, that the extreme top layer of sand, with its cover of slime, does the entire work, so far as purification is concerned. Each grain of sand of the body of the bed becomes covered with a sticky coating of the zoöglœa jelly, and these grains collectively are to be credited with a large share of the results accomplished.

A filter recently disturbed by the process of cleaning is

lower in efficiency than one which has been for some time in operation. Such a plant might be properly described as "at its best when at its dirtiest"; and, were it not that it finally becomes almost impervious to water, it would be better not to clean it at all. A new filter is of small use until it "ripens" for work; that is, until the "nitrifying" organisms have firmly established themselves and the zoöglœa jelly envelops the sand grains.

For proper working the thickness of the fine-sand layer should be made not less than thirty-six inches, and this depth should not be permitted greatly to decrease, by reason of the successive removals of layers of the upper surface for purposes of cleaning.

Usually filter plants are entirely open, but in those localities where the winters are severe it becomes necessary to throw over them a cover, which is commonly of concrete, resting upon columns of the same material. Thick ice renders it practically impossible properly to clean a filter by the ordinary methods, and the resulting imperfect purification of the filtrate is often coincident with increase in the death rate. This was noted in Berlin in the winter of 1889.

Hazen advocates the covering of filters in all localities where the mean January temperature is below the freezing-point.

The cost of constructing a filter bed must necessarily greatly vary, in direct ratio with the local cost of materials and with the difficulty of the engineering problem involved. Thus the open filters at Hamburg cost about $30,500 per acre, while the covered ones at Albany, N. Y., amounted to $45,600 for a like area.

The depths of water permitted upon filters of the English type are almost as various as the compositions of the beds themselves. Three and a half to four feet of water may be taken as the depth most commonly in use, and it is important that this depth, when once determined upon, should be maintained a constant.

With reference to the rate of filtration, the best practice places two and a half to three million United States gallons per acre per day, or four to four and a half vertical inches per hour, as the limit, beyond which the rate should not be pushed.

By direction of the imperial board of health, the maximum rate of filtration has been fixed in Germany at four vertical inches per hour.

For the purpose of cleaning a filter of the English type, a gang of laborers is set to work upon the drained bed, and by means of sharp shovels they pare off the upper half-inch of sand and pile the same into small heaps, whence it is removed by wheelbarrows to the sand washer. This thin upper layer of sand (the *Schmutzdecke* of the Germans) contains the greater bulk of the material separated from the water by filtration. It is quite compact, and is so distinctly separated from the sand below as to make the work of its removal very simple. It is liable to be quite membranous in character, and its imperviousness to water is what causes the filter to become "dead" and require cleaning.

The frequency with which filters have to be cleaned depends upon the condition of the water being filtered, and, for the same water, this condition will vary greatly with the time of year and character of the season. Roughly stated, it may be said that a filter becomes "dead" (*i.e.*, nearly impervious to water), and consequently demands cleaning, once every three or four weeks in summer and about half as frequently in winter; but it is not possible to lay down hard-and-fast general rules applicable to all filters. So many variable quantities enter the consideration that the question of proper time for scraping must be answered for each filter by itself, the final decision being based upon intelligent observation of the rate of flow, loss of head, and the obvious general efficiency. The average interval between scrapings at Albany is 25.1 days.

It is not customary nor desirable to have the newly scraped filter remain out of service until the sand removed is washed and returned to its place; for the fine sand layer should be thick enough to permit of a number of successive scrapings without impairment of its efficiency; therefore the sand taken off during a series of parings is all washed and returned at one time.

At Albany the sand layer, which is forty-eight inches thick, has been reduced as much as seventeen inches by successive parings before the normal thickness was restored by replacing the cleaned sand.

As to what may be expected from a sand filter in the way of bacterial removal, it may be said that during the year 1900 the Albany filters removed from 98.3 to 99.6 per cent. of all germs present in the raw water. Equally good results were accomplished by the beds at Altona, Germany, during the great outbreak of cholera at Hamburg in 1892. What such efficiency meant for the former city may be epitomized in the single word "safety."

It is not to be expected that municipal filtration plants will furnish the public with sterile water nor are we to look for perfect uniformity in bacterial efficiency, but it is a matter of fact that in those cities where modern filters have been established a very noteworthy reduction in the number of cases of typhoid fever has been observed. Thus in the city of Albany, where, previous to the introduction of filtered water, the average number of deaths from typhoid amounted to eighty-five per year, the influence of purified water is shown by a reduction of this number to less than twenty.

A modification of the English filter bed has been proposed, whereby filtration was to take place upward, and washing was to be done downward, the inlet for raw water and outlet for waste water being the same. By this arrangement the designer hoped to avoid all complications from ice, the ice cake being permitted to form freely and float clear of the sand bed. During washing a current of air was to have been let into the space underneath the bed, with a view to tumble the grains of sand and break up the sediment, so as to enable it to pass out with the wash water.

So far as principle is concerned, there may be little difference between upward and downward filtration, but in practice there would be serious objection to the former plan. Much difficulty would be experienced in securing uniformity of work over the whole area of the bed, owing to the impossibility of preventing the dirt layer falling off in spots, and it is well known that uniform action is of vital importance. It is moreover a dangerous practice to foul a filter in a place beyond reach of inspection and repair, for there is no way of determining whether or not the provided means of cleaning are working satisfactorily.

Mechanical Filtration.—Roughly outlined, this system consists in adding to the water to be filtered a minute dose of common alum or, better, aluminum sulphate, averaging nearly one grain per gallon, and then admitting the water to the filter, which is a tank of wood or iron, three-quarters full of uniformly fine sand. The carbonates present in the water decompose the alum, with the formation of a white flocculent precipitate of aluminum hydrate, quite jelly-like in appearance. For instance, the carbonate of calcium acts as follows:

$$Al_2(SO_4)_3 + 3CaCO_3 + 3H_2O = Al_2(OH)_6 + 3CaSO_4 + 3CO_2.$$

The action of this aluminum hydrate is much the same as that of the white of egg in clearing coffee. It entangles all suspended matter, germs as well as inorganic material, and deposits the same on the surface of the sand, whence it is removed and driven into the waste pipe by a reverse current of filtered water at the time of cleaning the filter. Thus, it will be observed, the mechanical filter produces an artificial inorganic jelly to replace the "bacterial jelly," already alluded to, of the English filter bed.

A further action of the precipitated aluminum hydrate is to unite with the soluble coloring matter of the water, whereby the filtrate is rendered colorless. The proper "dose" of alum solution is administered by means of some small automatic measuring apparatus exterior to the filter; the solution flowing thereto from the dissolv-

ing tank, where the coagulant is prepared in the proportion of twenty parts of water to one part of aluminum sulphate.

For small establishments it is a convenience to make use of a "closed" or "pressure" filter, for the reason that it can be placed directly upon the service main, thus allowing no interruption in the line of the supply. It is not easy, however, properly to watch such a filter, and it is open to sundry other objections, notably a lack of uniformity in action. For purposes of public use it is inferior to the open or "gravity" type.

The rate at which water is passed through these filters is very great when compared with what is furnished by the English filter beds already considered. One hundred and twenty-five million gallons per acre per twenty-four hours may be taken as a fair index of what is to be expected of them.

It has been already said that alum is used in their operation. The necessity for the use of this or some other coagulant is imperative and should be impressed upon the mind, for, however well the straining action of the sand bed may clarify the water, the great rapidity of flow precludes the proper removal of bacteria unless they be entangled in the alumina jelly noticed above.

Alum is by no means the only "coagulant" that could be or that has been used in mechanical filters. Salts of iron were suggested some years ago as a cheap substitute, but it is only recently that their use has been extended beyond the experimental stage.

What amount of coagulant should be used is a question best answered by the attendant in charge; for not only will the proper "dose" vary with different plants, but even in the same plant it may differ from day to day, and certainly will change from season to season. One grain per gallon is a fair estimate for a rough one.

It is worth remembering that theoretically a "dose" of one grain per gallon of aluminum sulphate (containing seventeen per cent. Al_2O_3) will require about eight parts per million of "alkalinity" in the water for its complete decomposition.

Danger to health from the use of alum is a topic fruitful of discussion among the many who are not posted as to its manner of action; but those who are better informed know that free alum never reaches the filtrate in a well-ordered plant.

Alum in the filtrate means a useless waste of material, not to be excused. Reference to the equation already given shows that in order to produce the aluminum hydrate jelly, upon which successful filtration depends, the alum admitted to the water must be entirely decomposed.

The method of testing for free alum is very simple, and the filter attendant, constantly on watch for it in the filtrate, should so manage the "dose" employed as never to allow it to pass beyond the sand bed.

The amount of filtered water used for the purpose of cleaning a mechanical plant is an item for consideration, for it is, of course, lost to the regular volume of supply. At Rensselaer, N. Y., the average run between cleanings is about twenty-four hours, and the filters are washed with 3.75 per cent. of the filtered water. It takes eight minutes to wash each "unit" or separate filter.

One feature of mechanical filtration that has come into prominence of late is the addition of some form of settling tank. With certain waters it is essential that opportunity be given for sedimentation of a portion of the heavy magma produced by coagulation, otherwise the sand bed quickly chokes and the labor and expense of cleaning are greatly increased.

When the water is so soft as to be deficient in the necessary quantity of carbonates to decompose the alum added, the bed of ordinary filtering sand is sometimes replaced by a mixture of such sand and granulated marble, or else the water is hardened by passing it over broken limestone previous to the addition of the alum. A better plan is to add a suitable dose of "soda ash" to the raw water.

Should the water be highly colored as well as soft, the addition of alum should immediately follow that of the carbonate and a considerable interval should intervene before the filter sand is reached, in order to allow complete reaction and partial sedimentation to take place. The time element is of special importance in the purification of such waters, and is to be secured by the erection of large settling basins.

The cost of erecting a mechanical filter plant is somewhat difficult to give, for the reason that patent rights enter the estimate. Perhaps the fairest general statement that can be made is to place $10,000 per million gallons daily capacity as the basis price for a first-class plant, and to subtract from that sum such concessions as the special features of the case may be able to secure.

Filters can be erected for half the above amount, and they do good work for manufacturing purposes; but their bacterial efficiency is low and the water used for washing will be from eight to ten per cent. of the delivery instead of about three per cent., as found in the best forms of apparatus.

The question so frequently asked, as to which of the rival systems of filtration it is better generally to adopt, is not capable of a direct answer. Local conditions must first be known. Slow sand filtration is likely to be the better for very large cities, while for the supply of towns the mechanical system is commonly preferable.

Either method of filtration, to be of value, requires constant attention. Careful watch must of necessity be kept of a mechanical plant, however small, to secure its running at all, while very inefficient supervision is the usual fate of the small English sand bed. Once constructed, it is commonly left to look after itself until cleaning is imperative, and then laborers are put upon the work who have never seen its kind before.

It is very doubtful policy to build an English sand bed unless the plant be large enough to maintain a skilled force constantly employed. It may be further generally said that, although relatively expensive for small plants, the English system rapidly lessens in cost, per unit of capacity, as the plant increases in size. This decrease is not so rapid for mechanical filters.

Other things being equal, English plants are perhaps better suited for clear waters, and mechanical filters for those of turbid or colored character.

The life of an English filter is practically unlimited, while that of the mechanical type is as yet undetermined.

Finally, it is an easier and cheaper matter to keep the mechanical filter nearer the present requirements as to capacity and to add to it by small extensions as circumstances may exact. So far as bacterial efficiency is concerned, either type will satisfactorily meet the demands.

Experiments of extended and costly character have been made with a view of securing data whereon to base a decision as to the merits of rival systems of filtration, and it is quite reasonable that the question should be asked, Why is it necessary to multiply such tests? Why cannot Louisville and Pittsburg results be made to do service elsewhere? To a large degree such use is possible, but it must be remembered that waters differ from one another more widely than the bulk of people appreciate. Thus the mere item of suspended matter is a case in point. Not only does the amount thereof greatly vary, but the character of the material causing the turbidity, and especially its degree of fineness, should command especial attention. Two equally turbid waters may look alike to the eye, but the fine suspended matter of one may be easily arrested by an English sand bed, while the other may give a filtrate of decided opalescence. Hence the demand for local experiments in important cases.

Nearly akin to the filter plants referred to above is a group of appliances among which the "Anderson process" is perhaps the best known. In this process the water is forced through purifiers consisting of iron cylinders revolving on hollow trunnions which serve for inlet and outlet pipes. On the inner surface of the cylinders are curved ledges running lengthwise, which scoop up iron borings or punchings and shower them down

through the water as it flows through the cylinder. Iron passes into solution and is afterward rendered insoluble by exposing the water to the atmosphere. By filtration through sand this iron precipitate is subsequently removed, together with what suspended matter it may have entangled.

Excellent results are secured by the Anderson process, but an additional and expensive step is introduced in the item of revolving machinery, before the water is run upon the sand filters; and it is not proved that this further outlay of capital is necessary, in view of the cheapness of some of the other and simpler methods.

Household filtration on the domestic scale is in very general operation, yet satisfactory results are obtained in an exceedingly small percentage of cases.

The companies manufacturing the mechanical filters previously mentioned all make sizes intended for domestic use, but the skilled labor furnished by a city employee whose sole duty it is to attend to the public plant is very rarely obtainable in the average household; consequently the filter is neglected or mismanaged, or both. In short, filtration, to be effectual, should be municipal. A house filter that has come widely into use, and upon which very many people pin their faith, is the well-known "Pasteur." It is commonly operated under the pressure of the city mains, but may also be arranged to work without additional pressure beyond that of the atmosphere. For those unacquainted with its use, it may be said that it consists of a cylinder of fine unglazed porcelain (called "candle," on account of its size and shape) enclosed by one of metal; and that, connection having been established between the latter and the supply pipe, the water is forced through the pores of the porcelain to the inside of the cylinder (the so-called candle), whence it drops into the reservoir, leaving the suspended matter as a coating upon the "candle's" exterior surface. (Fig. 5035.)

Fig. 5035. Pasteur-Chamberland Filter.

Examination of the efficiency of the Pasteur filter has been thoroughly done by a number of investigators, with results that may be summarized as follows: Water can be completely sterilized by filtration through porcelain, but the filtration must not be continued for many days at a time. The length of time during which a sterile filtrate may be obtained will depend upon the temperature of the filter and its contents. Thus, according to Freudenreich, at a temperature of 59° to 64° F. the filtrate was sterile for from fifteen to twenty-one days, at a temperature of 72° F. it was sterile during nine days, while at a temperature of 95° F. it remained sterile only five days.

Water pressure is not a factor in causing germs to pass through the porcelain, for their method of penetration is one of development rather than a transporting of initial bacteria; in other words, they "grow" through the filter. Even when the pressure is nil they accomplish the passage in the usual length of time. This power of growing through the pores of the porcelain has been denied by a recent observer, but it is on the side of safety to hold to the earlier records.

From a consideration of these facts the line of management for a "Pasteur" becomes plainly evident. The "candle" and its rubber packing must be removed at least once a week, thoroughly washed, and then boiled for half an hour before being reset in position.

Especial care should be taken that the rubber packing make a tight fit, as otherwise the water may pass around rather than through the porcelain. The filter should not be located in too warm a place.

The lateral connecting the filter with the supply main should be of tin or iron, as the slow action of the filter allows the water to remain for a considerable time in contact with the metal.

Many types of household filters are of such character as to preclude the possibility of sterilization, and some of them it is even impossible to clean without the entire renewal of the filtering material. Such defects are necessarily fatal to proper filtration. The stone filters one sees at times, where the water is caused to drip through fine-grained sand rock, or similar material, act as mere strainers and are absolutely unreliable. Currier demonstrated that sponge filters, after use for even a single day, furnished a filtrate containing five hundred times as many germs as the unfiltered water. Household filters of many types are to be seen so seriously contaminated that a water cannot but be rendered worse by passage through them, and yet such appliances are in full use and greatly trusted on account of the apparent clearness of the water drawn from them.

Much stress is often laid upon the purifying effects of animal charcoal, and the great quantity of occluded oxygen the fresh charcoal contains fully justifies for a time the high praise given it, but such material is nearly impossible to cleanse, and it has been repeatedly shown that a more objectionable appliance could scarcely be found, from a sanitary point of view, than a neglected charcoal filter.

Aeration of water has always held in the public mind a position of prime importance as a means of purification. There is unquestioned benefit arising from the passage of water over falls and rapids, and from its being thrown into the air in fountains, but the benefit is not so great as is commonly believed.

Such treatment tends to prevent the abundant growth of algæ, with their objectionable tastes and smells, and undoubted improvement in the quality of the water results from the establishing of a fountain in, or otherwise blowing air into, a too quiet reservoir; but the expectations of those who hope thus easily to eliminate pollution of a more serious character will not be realized.

Aeration is of especial value in rendering some kinds of ferruginous well waters, which are otherwise pure, fit for domestic use. The iron is thereby oxidized to insoluble ferric oxide, and may be easily removed by filtration.

In these days of "applied electricity," it would be strange indeed if attempts were not made to harness up the "fluid" for the work of water purification, as an addition to the many other tasks already assigned to it.

One movement toward such an end consists in decomposing a weak solution of common salt by means of a current from a dynamo, and then adding the electrolyzed liquid to the water to be purified, in the proportion of about 10 grains per gallon of water or 1 part to 5,833 by weight.

The product of the electrolysis is fancifully styled "electrozone," but the germicidal power which it possesses is due to the well-known sodium hypochlorite formed during electrolysis, and not to the presence of ozone.

The sodium hypochlorite prepared by this method is not different from that made in the ordinary way, and in germicidal power it is equalled by an equivalent weight of the calcium salt, called "bleaching powder," the efficiency of each being measured by the amount of available chlorine present.

The insoluble salts resulting from the employment of "bleaching powder" would, however, be a disadvantage in its use unless opportunity were afforded for settlement, and, moreover, it would render the water harder.

To "disinfect" a water by the use of hypochlorites does not appeal to one as a suitable means for increasing its potability.

The actual application of ozone in the form of ozonized air to the purification of water has a number of earnest supporters, and we await with interest the further development of such a process. Up to the present, how-

ever, it is right to say that the experimental stage is scarcely passed, although the flattering results secured by experiments permit us to entertain expectations of ultimate success.

From a sanitary standpoint, the method for purification of water which excels all others in efficiency is distillation. The peculiar taste of freshly distilled water is, however, disagreeable to many, and for that reason the process is not likely to become speedily popular, even if the expense be not too great.

It would seem that the attention of the public has been largely drawn of late to the question of the wholesomeness of distilled water for dietetic purposes, numerous articles having issued from the press under such captions as "Poisonously Pure Water" and the like. Much uneasiness has been created among those who have used such water, because of their being told that "distilled water is an active protoplasmic poison, due to its property of extracting salts from animal tissues and causing them to swell up by imbibition." Stress is, of course, laid upon the increased danger arising from its use by the young, whose tissues are in process of formation.

In consideration of the mixed character of human food and the amount of mineral salts naturally occurring therein and added thereto as condiments, the withdrawal of two or three grains of such salts per day, by the substitution of distilled water for that drawn from some natural source, would be a matter of too small importance for consideration.

Distilled water is used for drinking purposes on practically every vessel in the United States navy, and the surgeon-general says: "It may be stated that the medical officers of the navy recognize the great value of distilled water in the improvement in health that has followed its introduction, particularly on certain foreign stations."

The good old household remedy of boiling a suspicious water is always available, but unfortunately it is but seldom applied. As an illustration of its value it is worth noting that during the cholera outbreak at Lucknow, among the members of the East Lancashire Regiment, there was no cholera whatever in company E. This company was the only one which boiled the drinking-water.

Finally, let it be noted that there is no way of purifying a polluted water, as some people would have us do, by throwing a remedy into the well or cistern.

Water Analysis.—A great deal of popular misconception exists upon the subject of the analysis of potable water, and it is commonly supposed that such an examination may be looked upon from practically the same point of view as the analysis of an iron ore. In point of fact, however, it is a very different matter.

A water analysis is really not an analysis at all, properly so called, but is a series of experiments undertaken with a view to assist the judgment in determining the potability of the supply. Some of the substances reported, "albuminoid ammonia," for instance, do not exist ready formed in the water at all, and are but the experimental measures of the objectionable organic constituents, which our present lack of knowledge prevents our estimating directly.

It is not practicable to furnish the public with the means of fully understanding the numerical results as stated, nor is it possible to supply general "standards of purity" whereby a water may be rated as wholesome or otherwise, for the reason that figures which would condemn a water in one locality might be entirely without objection for a water derived from a neighboring county.

The examiner must be in full possession of all the facts concerning the water which he is asked to test, in order that his opinion as to its purity may be based upon the entire breadth of his past experience, for in no branch of analytical work are experience and good judgment better exercised than in the interpretation of a water analysis.

It is a great mistake to suppose that the proper way to consult a water expert is to send a sample of the water in a sealed vessel with no hint as to its source. On the contrary, he should be thoroughly acquainted with the history and source of the water and, if possible, he should take the samples himself. For so important a matter as a town supply, he should unquestionably personally superintend their collection.

Finally, let it be said that a water analysis is, for purposes of economy, rarely made complete. For ordinary drinking-water the question is always asked, "is it wholesome?" To answer this, the analysis of the mineral residue left upon evaporation is not usually required, so that much time and expense may be saved by simply reporting this as "total solids." On the other hand, analyses of mineral waters deal with this feature of the examination very largely, and usually to the exclusion of those portions, such as "albuminoid ammonia," "required oxygen," etc., which are important in the "sanitary analysis." The same may be said of the analyses of waters for boiler use.

Large glass-stoppered bottles are best for sampling. After thorough rinsing with the water to be analyzed, fill the vessel to overflowing so as to displace the air, and then completely empty it.

If the water is to be taken from a tap, let enough run to waste to empty the local lateral before sampling; if from a pump, pump enough to empty all the pump connections; if from a stream or lake, take the sample well out from the shore, and sink the stoppered sampling vessel toward mid-depth before removing the stopper, so as to avoid both surface scum and bottom mud. In every case fill the vessel nearly full, leaving but a small space to allow for possible expansion, and close securely. Under no circumstances place sealing wax upon the stopper, but tie a piece of cloth firmly over the neck to hold the stopper in place. The ends of the string may be afterward sealed if necessary. Having secured the sample, the analysis should be begun at once, for the reason that water is liable to rapid changes in character during laboratory storage.

The results of the chemical examination should be stated in "parts per million" in weight. Water should not be filtered before analysis. If sediment be present, it should be equally diffused by thorough shaking before measuring. The reason for this is that a water analysis should represent the water as the consumer uses it, and not in a condition improved by filtration.

The analysis cannot be properly conducted in a general laboratory, because many of the tests would be ruined by the fumes common to such a locality. A separate room, reserved exclusively for water work, is the best arrangement.

The appearance and turbidity of a water are best determined by using a brass tube two and one-half inches in diameter and two feet long, closed at the ends by discs of quarter-inch plate glass held in place by screw caps.

For the purpose of measuring the amount of turbidity, a standard is prepared, consisting of 1 gm. of exceedingly fine kaolin (obtained by elutriation) suspended in one litre of distilled water. Each cubic centimetre of this preparation will contain 1 mgm. of suspended clay. Having nearly filled the duplicate observation tube with distilled water, enough of the "clay standard" is added to make the "turbidity" equal to that of the water under examination in the other tube. Knowing the volume of water operated upon and the amount of "clay standard" used, the "turbidity" expressed in parts per million can readily be calculated. For more rapid although less accurate observations, the tubes above mentioned may be replaced by a number of half-gallon bottles, in which a series of turbidity standards are kept ready for immediate use.

As used by the United States Geological Survey, the turbidity standard is a suspension of silica (infusorial earth) of such a fineness that a bright platinum wire 1 mm. in diameter can just be seen when the centre of the wire is 100 mm. below the surface of water which contains in suspension one hundred parts of such silica per million parts of water. The turbidity of such standard is rated as 100.

A turbidity rod with graduations based upon this

standard is prepared for the survey and is very convenient for use in the field.

When variations in turbidity are being watched in a locality where the suspended matter is colored, the "clay standards" should be prepared from local material.

The reaction of natural water is commonly slightly alkaline, although waters holding much free acid in solution, usually sulphuric, are by no means rare.

Determination.—Place 100 c.c. of the water in a casserole, and titrate with N/10 hydrochloric acid, using methyl orange as an indicator. Should the water be originally acid, make it slightly alkaline with a known amount of potassic hydrate before titration. It is convenient to report alkalinity as representing so many parts of $CaCO_3$ per million of water, and to note that such a form of result corresponds to fifty times the number of cubic centimetres of hydrochloric acid, used in the titration.

Acidity is best stated in the same terms using a negative sign.

Color.—Dissolve 1,246 gm. potassic platinic chloride and 1 gm. cobalt chloride in 100 c.c. strong HCl and dilute with distilled water to 1 litre. This solution has a color of 500.

By placing one, two, three, four, etc., cubic centimetres of such solution in 50 c.c. "Nessler" jars and diluting to the mark with distilled water, standard colors of 10., 20., 30., 40., etc., are obtained, and with these is compared a 50 c.c. "Nessler" jar filled with the water under examination. Turbid waters should be filtered before reading the color.

Total Solids.—Material dissolved or suspended in water is naturally derived from the strata through which the water passes or the surface over which it flows. Thus are obtained waters of all degrees of hardness and of great variety of color and turbidity.

Determination.—Thoroughly shake the vessel containing the sample and then measure out 100 c.c. of the unfiltered water by means of a pipette into a weighed platinum dish. Evaporate to dryness on the water bath, being careful to place a filter paper between the dish and the water in the bath in order to prevent any deposit of impurities on the under side of the dish. (A better plan is to make use of a porcelain water bath filled with distilled water.) When dry, place the dish and contents in an air bath and maintain the temperature at 105° C. for half an hour. Cool in a desiccator and weigh.

Comparates.—Average in sundry surface waters known to be pure, 74; known to be polluted, 194; average in sundry ground waters known to be pure, 144; known to be polluted, 642.

These averages are really of but small sanitary value, for the reason that a polluted water may be low in total solids, or *vice versa*, according to the character of the soil through or over which the water flows.

HARDNESS.—Before entering into the question of quantitative estimation, let it be premised here that "hardness" may be classified under two heads, viz., "Permanent" and "Temporary." The former is occasioned by the presence of calcium sulphate and other soluble salts of calcium and magnesium, not carbonates, held in solution by the solvent action of the water itself; such a water cannot be materially softened by boiling under ordinary pressure.

"Temporary" hardness is caused by carbonates of calcium and magnesium held in solution by carbonic acid present in the water. Boiling such a water expels the carbonic acid, whereupon the salts separate from solution.

Hehner's method for determining "permanent hardness" is very convenient: The measured water is boiled down with a known excess of Na_2CO_3. Precipitated $CaCO_3$ is filtered off, and the remaining Na_2CO_3 determined by titration with standard acid and methyl orange. The loss in Na_2CO_3 is calculated to a corresponding amount of $CaSO_4$.

"Temporary hardness" is usually equal to the "alkalinity," previously determined.

Should sodium or potassium carbonates be present, the acid required to neutralize the water residue, after boiling down as above, will be greater than the amount corresponding to all of the standard Na_2CO_3 solution added, for no permanent hardness could be present in such a case. From such excess of acid the carbonates of the alkali metals can be calculated. Their equivalent in terms of $CaCO_3$ should be subtracted from the total "alkalinity" in order to state correctly the "temporary hardness."

Comparates.—The average hardness of good waters as given by the British Rivers Pollution Commission stands: Rain, 3; upland surface, 54; deep well, 250; spring, 185.

Chlorine.—Water is rarely found free from chlorine, yet, notwithstanding its almost constant presence, there is hardly a factor in the sum total of water analysis toward which attention is more quickly turned or regarding which there is closer scrutiny.

In most instances chlorine is present in the form of common salt, washed from the air or soil, or added as one of the constituents of sewage. Salt itself is, of course, unobjectionable in the quantity usually present, but, it being so largely used in our food, there is always warrant for suspecting sewage contamination where the figures for chlorine run high.

True it is that those figures are at times misleading, but they, like other data in water analysis, must be considered with judgment, and due weight be accorded the character of local surroundings.

If the district whence the water comes be naturally rich in salt, as is the case with the deep-seated waters of Central New York, such fact must be borne in mind when formulating an opinion as to quality. Variation in the chlorine contents of rain water always occurs inland, although not to the same degree as upon the coast. Ground water is more directly influenced than rain water by the presence of human habitation.

The determination of chlorine in water is extremely simple. It depends upon the fact that if to a solution of a chloride which has been colored yellow by addition of a little potassic chromate a solution of silver nitrate be added, white silver chloride will be produced until the last trace of chlorine shall have been disposed of, whereupon red silver chromate will begin to appear.

The reagents required are:

Standard Silver Solution.—Prepared by dissolving 4.8022 gm. of crystallized silver nitrate in 1 litre of water. Each cubic centimetre of such a solution is of a strength sufficient to precipitate 1 mgm. of chlorine.

Potassium Chromate, Indicator.—Dissolve 2 gm. of the pure salt in 100 c.c. of distilled water.

Sodium Carbonate Solution.—Dissolve 50 gm. of the pure salt in 300 c.c. of distilled water.

Determination.—One hundred cubic centimetres of the water to be examined are placed in a large "Nessler" jar; 1 c.c. of the potassic chromate solution is added, which will give a distinct yellow color, and then the standard silver solution is run in from a burette until the red tint of the silver chromate just appears. From the known amount of silver solution used the amount of chlorine present is obtained, and this, multiplied by ten, will give the chlorine in milligrams per litre or parts per million.

To determine with accuracy the first appearance of the red tint, it is best to make the examination in yellow light, either by the use of a photographic "dark-room" lantern with a front of yellow glass or by simply looking through a plate of such glass. Reflection from a porcelain tile throws the light through the length of the "Nessler" jar, and side light is cut off by a black screen.

For the sake of accuracy it is better, during the titration, to have a second jar of the water, also colored with potassic chromate, in order that the formation of the red tint in the vessel operated upon may be, by contrast, more readily detected.

Many waters possess such deep color or such turbidity as to interfere with proper titration; under such circumstances it is best to shake the water with recently precipitated and washed aluminum hydrate and then filter it,

or allow it to stand twenty-four hours in a tall glass cylinder. The coloring matter or turbidity is thus sedimented and the water cleared for use.

Comparates.—Average in sundry surface waters known to be pure, 3.57; known to be polluted, 6.06; average in sundry ground waters known to be pure, 3.2; known to be polluted, 91.7.

NITRITES.—Whether the presence of nitrites be considered due to reduction of pre-existing nitrates in the presence of organic matter or caused by direct oxidation of organic nitrogen, it becomes a necessity to estimate their quantity, for in either case the initial cause is probably contamination.

Of the several methods used of late for the determination of nitrites, the second one suggested by Griess seems to be the most deserving of favor. It depends in principle upon the red coloration ("azobenzolnaphthylamine sulphonic acid") produced whenever "sulphanilic acid" and "naphthylamine hydrochloride" are added to an acidified solution of nitrite. The test is exceedingly delicate and is capable of distinguishing one part of nitrogen as nitrous acid in one thousand million parts of water.

The reagents are prepared as follows:

Sulphanilic Acid.—Dissolve 1 gm. of the salt in 100 c.c. hot water. The solution keeps well.

Naphthylamine Hydrochloride.—Boil 0.5 gm. of the salt with 100 c.c. water for ten minutes, keeping volume constant. Place in glass-stoppered bottle. The solution tends to grow slightly pink on standing, but not sufficiently so to interfere with its use.

Standard Solution of Sodium Nitrite.—Sodium nitrite may be bought, but its purity is always to be questioned, and, moreover, it is too deliquescent a salt to be weighed with ease and accuracy. It is better, therefore, to prepare the silver salt, which may be readily handled, and from it the solution required may be made.

To a cold solution of commercial sodium or potassium nitrite add a solution of silver nitrate as long as a precipitate appears. Decant the liquid and thoroughly wash the precipitate with cold water. Dissolve in boiling water. Concentrate and crystallize the silver nitrite from the hot solution. Dry in the dark at the ordinary temperature (using vacuum is better) and keep it in a black bottle.

Weigh out 0.22 gm. of the dry silver nitrite. Dissolve in hot water. Decompose with slight excess of sodium chloride, cool if necessary, and dilute to 1 litre. Allow the precipitated silver chloride to settle, remove 5 c.c. of the clear solution, and dilute the same to 1 litre. This second dilution (which is the standard solution to be used) will contain an amount of nitrite per cubic centimetre equivalent to 0.0001 mgm. of nitrogen.

Determination.—Place 100 c.c. of the water to be examined in a "Nessler" jar. Acidify with one drop concentrated HCl. Add 1 c.c. of the sulphanilic-acid solution, followed by 1 c.c. of the solution of hydrochloride of naphthylamine, mix, cover with watch glass, and set aside for thirty minutes. Prepare at the same time other "Nessler" jars containing known amounts of the standard solution of sodic nitrite and diluted to the 100-c.c. mark with *pure* distilled water, adding the reagents as above. At the end of the time stated (thirty minutes) examine the depth of the pink color formed, and by comparing the unknown with the known an accurate determination of the amount of nitrogen present as nitrites may be made.

If much gas be burning in the room, nitrites will be in the atmosphere. Hence cover the jars or remove them from the room during the half-hour interval before reading.

Nitrites are sometimes found in deep-well waters of good quality, but in ground or surface waters their presence should be always regarded with suspicion.

Comparates.—Average in sundry surface waters known to be pure, 0.000; known to be polluted, 0.006; average in sundry ground waters known to be pure, 0.000; known to be polluted, 0.003.

NITRATES.—Nitrates present in water are but the further step in the oxidation of nitrogenous organic matter. They are more liable to indicate putrefaction of animal rather than of vegetable tissue, not only because of the greater quantity of nitrogen present in the former, but also on account of its more ready decomposition.

Rain water washes a very considerable amount of nitric nitrogen from the air, while in the soil the atmospheric nitrogen is fixed through the agency of the roots of certain plants, such as peas, the process being aided by bacterial action.

Such fixed nitrogen eventually enters the ground water, and a knowledge of the local "normal" for nitric nitrogen is consequently of advantage when studying the domestic well waters of a neighborhood.

Surface and ground waters of good quality are low in nitrates, for the reason that such material is quickly absorbed by growing vegetation, but waters from deep wells often give large figures for that item.

When phenolsulphonic acid is brought in contact with a nitrate, and ammonia is afterward added to alkaline reaction, yellow ammonium picrate is formed.

The intensity of this yellow color, produced in the water under examination, is compared with colors of known strength, and the quantity of nitrate present thus determined.

The interference of chlorides with this process results in readings lower than the truth, but if the chlorine be below ten parts per million such interference is not material.

The solutions required are:

Phenolsulphonic Acid.—Sulphuric acid, pure and concentrated, 148 c.c.; distilled water, 12 c.c.; pure phenol, 24 gm.

Standard Potassium Nitrate Solution.—Dissolve 0.7221 gm. pure KNO_3 in 1 litre distilled water. This solution contains 0.1 mgm. of nitrogen as nitrate in each cubic centimetre.

Determination.—Evaporate 100 c.c. (or less, according to nitrate contents) of the water to dryness on the water bath, having previously added a few drops of sodium carbonate solution to prevent loss from volatilization of nitric acid. Thoroughly moisten the residue with 2 c.c. of the sulphonic acid. Add an excess of ammonium hydrate. Make up to 100 c.c. in a "Nessler" jar, and compare the depth of color with those produced by operating upon different amounts of the standard nitrate solution, which have been evaporated and treated under precisely similar conditions.

In order to economize time, when dealing with waters low in chlorine, it is convenient to use a standard "nitrate color solution." This is made by evaporating 25 c.c. of the standard potassium nitrate solution, followed by addition of the other reagents in the way already detailed.

The yellow liquid produced is diluted to 1 litre and kept in stock. Each cubic centimetre thereof corresponds to 0.0025 mgm. nitrogen as nitrate. Much time is saved by diluting measured volumes of this "standard color" to 100 c.c. for the preparation of the comparison tubes.

The solution keeps its normal strength of color quite well, but should not be trusted after having been a few weeks in stock.

Before evaporating for the nitrate determination it is best to clear the water with aluminum hydrate as under "chlorine."

Comparates.—Average in sundry surface waters known to be pure, 0.139; known to be polluted, 0.749; average in sundry ground waters known to be pure, 1.4; known to be polluted, 11.9.

Mallet found in thirteen samples of water "known to be pure" the nitrogen present as nitrates averaged 0.42 (the extreme limits being 0 and 1.04), while in twenty samples of water believed to be objectionable the average figures ran 7.239 (the extreme limits being 0 and 28.403).

Organic Matter.—It is here that water examination loses its analytical features and becomes experimental in character. Organic matter cannot be determined directly

and we are forced to resort to certain lines of procedure which experience has taught us differentiate more or less sharply between good and bad waters, even though the actual composition of such waters be not thereby revealed.

Organic matter containing nitrogen, when breaking down through putrefaction, liberates its nitrogen as ammonia, and this in turn changes to nitrites and nitrates of the bases present. The ammonia formed, as above, may be separated from the water by simple distillation and when determined is reported as "free ammonia." Such of the nitrogenous organic matter as yet remains undecomposed may be in great part broken up, and its nitrogen given off as ammonia, by distillation with strongly alkaline potassium permanganate. This second evolution of ammonia is called "albuminoid," for the reason that albumin acts in like manner when similarly treated. Wanklyn's "albuminoid ammonia process" is based upon the foregoing facts.

The reagents necessary are:

"*Nessler's*" *Solution.*—Dissolve 16 gm. mercuric chloride ($HgCl_2$) in about half a litre of pure water. Dissolve 35 gm. potassic iodide (KI) in about 200 c.c. pure water. Pour the first solution into the second until a faint show of excess is indicated. Add 160 gm. solid potassium hydrate (KOH). Dilute to 1 litre, and finally add strong solution of mercuric chloride, little by little, until the red mercuric iodide just begins to be permanent. Do not filter from excess of mercuric iodide, but let the same settle to the bottom of the vessel. The finished reagent should have a pale straw color. It is improved by age.

"Nessler's" solution will give a distinct brownish-yellow coloration with the most minute traces of ammonia or ammonium salts. If the quantity of ammonia be at all considerable, a brown precipitate will appear.

Pure Water.—This must be prepared with great care, in a room free from the usual laboratory fumes. In short, the entire examination of potable water should be undertaken in a locality other than a general working laboratory. The most suitable retort for this purpose is of copper, three gallons in size, and with a tin condensing worm. Fill it with good spring water, distil, collect distillate in 50-c.c. "Nessler" jars, and to each successive jarful so collected add 2 c.c. "Nessler" solution. After waiting five minutes, should a brown tint be observed upon looking through the liquid (*longitudinally*) at a white porcelain tile or piece of white paper, the presence of ammonia is indicated.

Continue the distillation and the "nesslerizing" of the successive 50-c.c. portions of the distillate until no coloration is obtained even after standing for five minutes. When ammonia ceases to be detected, the distilled water may be collected for use. The distillation should not be pushed too far, both on account of danger to the retort and of possible production of ammonia from decomposition of the organic material remaining in the bottom.

Alkaline Potassic Permanganate.—Dissolve 200 gm. solid potassic hydrate and 8 gm. crystallized potassic permanganate in 1,250 c.c. of pure water. Boil down to 1 litre and keep for use.

Sodic Carbonate Solution.—Dissolve 50 gm. of the pure salt in 300 c.c. pure water.

Standard Ammonia Solution.—Dissolve 1.5706 gm. of pure dry ammonium chloride in half a litre *pure* water. Dilute 5 c.c. of this solution to half a litre with *pure* water. This second solution will represent a strength of 0.01 mgm. of NH_3 per cubic centimetre, and is the standard solution used.

Determination of Free Ammonia.—Fit a one-quart glass tubulated retort to a large Liebig condenser, letting the neck of the retort pass well into the condensing tube and through a large-size soft-rubber stopper. This connection must be thoroughly tight. Place 250 c.c. *pure* water in the retort and add 10 c.c. of the sodic carbonate solution. Distil off three 50-c.c. jars of water, and "nesslerize" the third in order to be sure that no ammonia yet remains in the retort. Any ammonia that may have resulted from the imperfect cleaning of the apparatus, or that may have been present in the sodic carbonate solution, will usually all go over in the first 50 c.c. of distillate, but the same quantity (*i.e.*, 150 c.c.) must be distilled off in all cases in order that when the actual analysis of the unknown water is started upon the condition as to volume may be constant.

In fact, it may be conveniently stated here that *perfect uniformity of conditions* is a requisite for success in water analysis.

To the contents of the retort is now added half a litre of the water to be examined.

Distil and catch the distillate in 50-c.c. "Nessler" jars. The rate of the distillation should be so managed as to allow about fifteen minutes for the filling of each 50-c.c. jar. Add 2 c.c. "Nessler" reagent to each jarful, and continue the operation with each successive portion of the distillate until no further reaction for ammonia is apparent after waiting five minutes. Usually four jars will be sufficient to carry off all free ammonia, but it is customary to distil off six.

From a small burette measure definite amounts of the *standard ammonia solution* into several clean "Nessler" jars. Dilute each to the 50-c.c. mark with pure water, add 2 c.c. "Nessler" solution, and after standing for five minutes compare as to depth of tint with the distillates already "nesslerized." With a little practice it will be found easy, by varying the amounts of standard ammonia solution used, to produce tints corresponding to those existing in the distillates, and thereby a most accurate knowledge of the quantity of ammonia actually present may be obtained. Such ammonia existed ready formed in the water, either free or as an ammonium salt, and passed over unchanged with the steam; it is therefore technically known as "*free ammonia.*"

To make clear the calculation of results let us cite an example: Suppose the first jarful to have required 9 c.c. standard ammonia solution (diluted to 50 c.c.) to match its color when "nesslerized," the second one 3 c.c., and the third 1 c.c. Then, since each cubic centimetre of the standard ammonia solution corresponds to 0.01 mgm. NH_3, the whole amount of "free ammonia" present in the original half-litre of water would be: First, 0.09 mgm.; second, 0.03 mgm.; third, 0.01 mgm.; fourth, 0.00 mgm.—total, 0.13 mgm. Multiplying this by two to obtain the quantity for an entire litre, and remembering that 1 mgm. is the millionth part by weight of a litre of water, we find the total "free ammonia" present in the water to be 0.26 *part per million.*

Albuminoid Ammonia.—Throw out the residue remaining after the distillation for *free ammonia*, clean the retort thoroughly, and refit it to the condenser. Place in the retort 200 c.c. pure water and 50 c.c. of the *alkaline permanganate solution.* Distil off three 50-c.c. jars and "nesslerize" the third one in order to insure freedom from ammonia. Add half a litre of the water under examination, and proceed with the distillation and the "nesslerizing" of the successive 50 c.c. portions of the distillate, as in the determination of *free ammonia.* The distillation is to be continued until six 50-c.c. jars are filled. The ammonia determined by this distillation will be *total* (*i.e.*, "free" plus "albuminoid"); therefore from the Nessler reading of each jarful of distillate must be subtracted the reading for the corresponding jarful for "free ammonia"; the difference will give the "albuminoid ammonia" for that jar.

The calculation is entirely similar to that for *free ammonia*, as stated.

Concerning the interpretation of results, Wanklyn is very dogmatic, and says: "The analytical characters, as brought out by the ammonia process, are very distinctive of good and bad waters, and are quite unmistakable." This statement is altogether too strong. Waters of high organic purity or those of gross pollution are undoubtedly easy to classify, but with the numerous cases which lie about the boundary line between "good" and "bad," the greatest care is to be exercised in the reading of results and the passing of judgment.

As an illustration of variation in the ammonias, the following data are offered:

	Free ammonia.	Albuminoid ammonia.
Average in sundry surface waters known to be pure	0.063	0.066
Average in sundry surface waters known to be polluted	.182	.228
Average in sundry ground waters known to be pure	.009	.007
Average in sundry ground waters known to be polluted	.107	.081

The "free ammonia" in artesian wells is often excessive, under circumstances that make animal contamination an impossibility, and even rain water, freshly collected after periods of long drought, will often exhibit properties calculated to mislead the analyst.

Free ammonia is at times very high in the rain water collected near large cities, and is liable to run higher in winter than in summer. Of course high figures under such conditions are without objection, assuming a clean roof and a clean cistern; but when dealing with a rain water it must be always borne in mind that storage cisterns are often very foul.

As a further aid to judgment the following analyses are given of sundry waters in different parts of the country, several of them having caused disease. Also a few instances of waters of reliable quality.

No.		Free ammonia.	Albuminoid ammonia.	Chlorine	N as nitrate.	N as nitrite.	Required oxygen.	Total solids.
	Impure.							
1	Shallow city well	.025	.08	122.0	17.38	Trace.	1.4	554.0
2	City well 30 feet deep (caused typhoid)	.065	.035	146.0	10.0	.0	1.0	769.0
3	Rock-drilled city well 76 feet deep	2.025	.0	10.0	.025	.0	.85	487.0
4	Spring-water (caused repeated cases of dysentery	.01	.025	6.0	7.0	.0	.8	35.0
5	Well near city	.005	.045	24.0	9.0	.0	1.1	215.0
6	Country well, strong salty taste	.59	.245	2,803.0	. .	.25	. . . .	5,225.0
7	Town well	.815	.075	8.0	.0	Trace.	.....	421.0
8	City well 250 feet deep	1.59	.395	1.2.0	.0	Trace.	.....	681.0
9	City well 555 feet deep	.31	.02	58.0	.0	.0	6.45	635.0
10	City well 226 feet deep	1.11	.08	199.0	.0	.0	1.3	779.0
11	Deep well in large stock-yard, Kansas City	1.745	.025	80.0	.0	Trace.	.....	.....
12	Hudson River, at Troy, during freshet	.42	1.0	3.0	.5	Trace.	.....	205.0
13	Deep city well, in "made ground"	Excessive.	Excessive.	47.0	.875	.0	2.5	637.0
	Pure.							
14	Peaty mountain stream (autumn)	.055	.23	2.4	.0	.0	7.4	34.0
15	Same stream in winter	.055	.117	1.9	.08	.0	6.6	47.5
16	Mountain spring	.04	.048	4.0	1.404	Trace.	.3	228.0
17	Town supply, Elizabethtown, N. Y.	.048	.002	1.05	.05	.0	.35	106.0
18	Large well-situated spring	.027	.006	2.2	1.6	.0	.0	90.0
19	High mountain lake (peaty)	.01	.34	2.0	.0	.0	6.6	43.0
20	Lake Erie (middle of lake)	.045	.112	3.5	.08	Trace.	1.25	134.0
21	Lake Superior (forty miles from shore)	.03	.02	1.0	.1	.0	1.15	54.0
22	Flowing wells (New Jersey coast)	.023	.05	9.0	5	Trace.	.4	30.0
23	Driven wells (Hempstead, N. Y.)	.013	.004	2.5	1.25	.0	.35	22.0
24	Domestic well (Catskill Mountains)	.016	.007	.75	.175	.0	.35	32.0

Oxygen-Consuming Capacity ("Required Oxygen").—This method for estimation of organic matter is Kubel's modification of the old permanganate process of Forschammer. The necessary solutions are.

Standard Potassic Permanganate Solution.—Dissolve 0.3952 gm. of the salt in 1 litre of distilled water Each cubic centimetre of such solution will contain 0.1 mgm. of oxygen available for oxidation. The available oxygen of the permanganate in presence of sulphuric acid may be represented by the equation

$$K_2Mn_2O_8 + 3H_2SO_4 = K_2SO_4 + 2MnSO_4 + 3HO_2 + 5O.$$

Dilute Sulphuric Acid.—One part of the strong acid to three of distilled water.

Solution of Oxalic Acid ($H_2C_2O_4.2H_2O$).—Dissolve 0.7875 gm. of the crystallized acid in 1 litre of distilled water. This solution if titrated against the permanganate solution (while hot, and in presence of H_2SO_4) should correspond to it cubic centimetre for cubic centimetre. In practice, however, this correspondence will be found to be approximate only.

The solution tends to grow weaker quite rapidly with lapse of time, and must be restandardized every time it is used. This is, however, but a slight inconvenience, and is accomplished as follows:

Ten cubic centimetres of the oxalic-acid solution, diluted with 200 c.c. pure water and 10 c.c. of the dilute sulphuric acid, are titrated, boiling, with the standard potassic permanganate solution, and the amount of the latter required to produce a faint pink tinge is recorded.

Determination.—Place in a porcelain casserole 200 c.c. of the water under examination, and add 10 c.c. of the dilute sulphuric acid. Heat rapidly to incipient boiling, and run in the standard permanganate solution from a burette until the water has a very marked red color. Boil *ten minutes*, adding more permanganate from the burette from time to time, if necessary, in order to maintain the intensity of red color observed at the start. Do not let the color fade nearly out, and then add the permanganate in quantity at once, but strive to keep the color as nearly constant as possible by gradual addition.

Remove the lamp, add 10 c.c. (or more, if necessary) of the oxalic-acid solution to destroy the color, and then add the permanganate solution from the burette until a faint pink tinge again appears. From the total permanganate used deduct that corresponding to the 10 c.c. (or more) oxalic acid employed, and from the remainder calculate the milligrams of "required oxygen" consumed by the organic matter present in the water. Correction must be made for nitrites, ferrous salts, or hydrogen sulphide if any of them be present.

Example:

Total permanganate solution used	25.0 c.c.
Less that required for the oxalic acid	9.7 c.c.
Hence that required to oxidize organic matter	15.3 c.c.

Corresponding to 1.53 mgm. oxygen.

Therefore "required oxygen" is $1.53 \times 5 = 7.65$ per million.

Comparates.—As this determination deals principally with the organic carbon present, the readings are naturally high in the cases of brown peaty waters, and surface waters carrying organic matter in suspension. (See the list of analyses given above.) Average in sundry surface waters known to be pure, 1.58; known to be polluted, 3.00; average in sundry ground waters known to be pure, 0.31; known to be polluted, 1.06.

Lead and Copper.—It at times becomes necessary to examine water for these poisonous metals, and the ease with which their dark sulphides may be formed provides a ready method (Miller).

Prepare a standard solution of lead nitrate, $Pb(NO_3)_2$, by dissolving 1.5990 gm. of the salt in 1 litre of distilled

water. Each cubic centimetre will contain 1 mgm. metallic lead.

Place the water in a 100-c.c. "Nessler" jar; add four drops of concentrated HCl, followed by 1 c.c. of colorless ammonium sulphide, and match the tint by operating in a similar manner with measured amounts of the standard lead solution diluted to 100 c.c. This will not, of course, distinguish between copper and lead, but, inasmuch as either is objectionable, distinguishing is not commonly necessary.

In order to test the action of the water upon *lead pipe*, permit it to remain in contact with both bright and dull lead (in separate vessels) for twenty-four hours, and then examine the water as above.

Iron.—This metal is objectionable if in considerable quantity, particularly in water to be used for washing white goods and for dyeing. A knowledge of the presence of iron will, moreover, aid in guarding against an invasion of iron-secreting organisms such as crenothrix.

To determine its quantity acidify a suitable volume of the water with aqua regia; concentrate to 100 c.c.; place in a 100-c.c. "Nessler" jar; add 2 c.c. of ammonium sulphocyanate solution, and compare the depth of color produced with known amounts of standard iron solution diluted to 100 c.c. and similarly treated with ammonium sulphocyanate solution.

The *standard iron solution* is prepared by dissolving 0.1 gm. pure iron in a little HCl to which a few drops of HNO_3 have been added, and then diluting to 1 litre.

Alum.—When examining the effluent from mechanical filters, it becomes essential to determine if any undecomposed coagulant (*i.e.*, alum) passes into the filtrate. For such purpose the "logwood test" is by far the most valuable.

Boil some logwood chips in a little water for a few minutes and drain off the resulting extract. Repeat the boiling and again discard the extract. Boil for the third time about fifteen minutes and keep the extract for use.

Place about 100 c.c. of water in a porcelain dish, add a little of the logwood extract, followed by a little acetic acid. If even a trace of alum be present in the water a violet tinge will be obtained, which will not be discharged upon addition of the acetic acid. A "blank" should always be run for comparison. The logwood extract is reliable but for a short time, especially if exposed to air. It is never safe to trust it when more than a day old.

Logwood for this test cannot be readily purchased, that obtainable from the druggists being absolutely worthless. The best method of obtaining it is personally to bore the chips from the centre of the log.

When examining the filtrate from a mechanical plant by the logwood test, it would be well to take the alkalinity also.

If the filtrate be alkaline free alum cannot be present, and the logwood reaction, if then found, is due to particles of $Al_2(OH)_6$ passing the sand bed and becoming dissolved in the reagents employed.

Lacmoid should be used as the indicator, as methyl-orange does not indicate an acidity due to alum.

Bacteriological Examination of Water.—For the accomplishing of the determinations that are here proposed, the following culture media should be carefully prepared and kept ready at hand.

Bouillon.—Take one pound of lean beef, chop it fine, and let it soak overnight in 700 c.c. water in a cool place. Strain through a cloth with the aid of gentle pressure and make up to 1 litre with water. Add 10 gm. of peptone (Witte's) and 5 gm. of common salt. Heat in a double-walled "oatmeal-boiler" until the added ingredients are dissolved. Should the medium not be clear, cool somewhat, add the white of an egg, bring to a boil without stirring, and filter while hot.

The proper reaction of the finished medium should be about + 15 (*i.e.*, an acidity equal to what would be produced by the addition of 15 c.c. of normal hydrochloric acid to 1 litre of the medium made neutral to phenolphthalein).

In order to secure such a reaction place 5 c.c. of the medium in a porcelain dish, add 45 c.c. distilled water and 1 c.c. of a solution of phenolphthalein (0.5 gm. phenolphthalein in 100 c.c. of fifty-per-cent. alcohol).

Titrate to the neutral point with N/20 NaOH or with N/20 HCl (the former will be the solution most commonly required), and from these data calculate the amount of normal HCl required to be added to the bulk of the medium in order to bring it to the desired degree of acidity, namely, + 15.

The said normal acid having been added, the "bouillon" is placed in test tubes plugged with cotton or in flasks similarly closed; the cotton plug is then covered with a small sheet of "tinfoil" to prevent evaporation, and sterilization is accomplished by heating in an "Arnold's sterilizer" for twenty minutes on three successive days.

Sterilization may be accomplished by a single heating in an autoclave to fifteen pounds pressure for fifteen minutes.

Keep the "stock bouillon" and all other stock media in a cool, dark place.

Nutrient Gelatin.—Take one pound of lean beef, chop it fine, and let it soak overnight in 700 c.c. distilled water in a cool place. Strain through a cloth and make up to one litre with distilled water. Add: Gelatin (best French), 120 gm.; peptone (Witte's), 10 gm.; common salt, 5 gm. Heat in a double-walled "oatmeal-boiler" at a temperature between 35° and 40° C. until all is dissolved. Add the white of one egg, previously shaken up with about its own bulk of water, and stir thoroughly. Heat as rapidly as possible to boiling, stirring occasionally. Cover the mixture and keep the water in the outer vessel boiling during fifty minutes.

Filter, with the use of the hot-water funnel. Place 5 c.c. of the filtered medium in a porcelain dish; dilute the same with 45 c.c. water; titrate with N/20 NaOH solution, as in the case of the preparation of "bouillon," and from the data so obtained calculate what addition of normal HCl should be made to the main bulk in order to carry its reaction to the desired point, namely, + 15.

Pour the finished jelly into "Miquel" flasks or test tubes (10 c.c. in each). Plug the vessels with cotton and sterilize them in an Arnold's sterilizer for *twenty minutes* on three successive days or by a single heating in an autoclave at fifteen pounds pressure for fifteen minutes.

Sugar Bouillon.—Prepared the same as the ordinary "bouillon" except that 10 gm. of pure glucose are added with the peptone and salt. Its reaction should be neutral.

Inasmuch as the high temperature of the autoclave might partly decompose the sugar, it is better to sterilize in the Arnold's sterilizer for twenty minutes on three successive days. The best vessels in which to store "sugar bouillon" are the "Smith's fermentation tubes" in which it is to be used.

Sugar Gelatin.—Prepared like nutrient gelatin except that 10 gm. of pure glucose are added with the other ingredients. Sterilize in the Arnold's sterilizer for twenty minutes on three successive days. It is best kept in test tubes plugged with cotton; 10 c.c. in each tube.

Agar-agar.—Although plate cultures for water examination are best made by the use of "nutrient gelatin," it is sometimes convenient to employ a medium with a higher melting point. It must be noted, however, that "counts" of colonies growing upon agar must not be compared with those upon gelatin; the latter medium being more favorable to an increased growth.

To make 1 litre of agar-agar take: A. Chopped meat, 500 gm.; water, 500 c.c. Mix and place in cool place overnight, then strain through cloth. Add: Peptone (Witte's), 10 gm.; common salt, 5 gm. B. Agar-agar, 12 gm.; water, 500 c.c.

Place B in autoclave, run up to about thirty pounds of pressure, put out flame, and allow to cool until below 100° C. before opening. Let the solution of agar cool still further to about 75° C., and then mix A and B. Bring to a boil for about three minutes, neutralize, and

filter. The product is an absolutely clear jelly, which never forms any precipitate. (*Ravenel's method.*)

Place the finished medium in tubes and "Miquel flasks" and sterilize as usual.

Nitrate Solution.—Dissolve 1 gm. of peptone and 0.2 gm. of KNO_3 in a litre of water. Place the solution in cotton-plugged flasks (50 c.c. in each) and sterilize.

Dunham's Solution.—Dissolve 10 gm. of peptone and 5 gm. of NaCl in a litre of water. Place the solution in cotton-plugged flasks (50 c.c. in each) and sterilize.

Empty glassware is best sterilized by a single heating for one hour to 170° C.

The pipettes used for the measurement of the water should be plugged with cotton near the end which is placed in the mouth; the whole pipette should then be placed in a suitable glass tube containing a cotton plug in its open end.

Water samples for bacteriological purposes are most conveniently taken in bulbs of glass with long thin stems, similar to the stock article in use for specific-gravity determinations. These bulbs can be sterilized by the direct Bunsen flame and sealed while hot. Upon afterward breaking off the point of the stem under water the water will enter the vessel because of the partial vacuum, and the stem can be at once resealed by using a candle flame and a blowpipe. Such bulbs are very convenient for taking deep samples, as the point of the stem can be broken by a separate string while the bulb is held by the sinking apparatus. During transportation the bulbs filled with water samples should be packed in ice.

Upon arrival at the laboratory 1 c.c. or less of the water, after thorough agitation, is transferred, by means of a sterilized pipette, to a sterile Petri dish. A tube of culture jelly (the jelly having been previously liquefied by immersing the tube in warm water at 35° C., and the open end of the tube having been held for a moment in the Bunsen flame) is then quickly poured into the Petri dish, and mixing is accomplished by tilting the dish forward and back. After the jelly has again hardened the dish should be maintained, in the dark, at a temperature of about 22° C.

When "agar" is employed it is more convenient to melt it at 100° C. and then cool it to about 40° C. before sowing.

Each individual bacterium, finding itself embedded in material supplying abundance of food, proceeds to surround itself by a multitude of its offspring, until at length the "colony" so produced becomes large enough to be seen by the naked eye. These colonies, each of which corresponds to one original bacterium, are of various sizes and shapes. Some of them do, and others do not, liquefy gelatin.

The method of sowing water samples as given above is that in common use, but preference is sometimes given to the use of conical "Miquel" flasks, usually two and one-half inches in diameter at the bottom, with a tubulated glass cap, ground at the joint (Fig. 5036). The tubulation is plugged with cotton. Such flasks receive 10 c.c. each of the culture jelly when it is first made, and are kept in stock like the test tubes. Taken to the field, they receive, on the spot, the measured amount of water, and the chances of contamination during transfer of the Petri dish and of multiplication during the journey of the water sample to the laboratory are thereby avoided. This method of working has proved very satisfactory, as no transportation of the water sample is required.

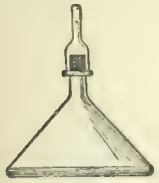

FIG. 5036.—Miquel Flask.

In place of sowing a fraction of a cubic centimetre of water, the "dilution method" conduces to greater accuracy. One cubic centimetre or 10 c.c. of the water are diluted to 100 c.c. with sterilized water and then 1 c.c. of the mixture is sowed in the medium. This is Miquel's favorite method. Of course this dilution must be done with great care, as any error is multiplied.

Counting the colonies of bacteria is undertaken forty-eight hours after the sowing, according to the official German regulations, but it is well to delay it longer or to count sooner, according as the danger may be less or greater of the colonies growing into each other and thus confusing the count.

Of course, what is required is the maximum count, and good judgment must be exercised as to when is the best time to secure it. For purposes of comparison (and usually comparison examinations are the most important form of water investigations) four days will be found a convenient interval between the sowing and the final counting of the colonies. When the number of the colonies is large, counting must be done with the aid of a ruled glass plate.

Sundry bacteria are capable of inducing a fermentative action, with evolution of gas (CO_2 and H), when sown in a medium containing one per cent. of glucose. The *Bacillus coli communis* is a prominent member of this group, and the persistent presence of many of these germs in a water is strong evidence of its contamination by intestinal products from man or the higher animals.

Tests for B. coli communis.—1. To each of ten Smith's "fermentation tubes," charged with sterile "sugar bouillon," add 1 c.c. of the water. Mix by tilting the tube, and place in the incubator at 38° to 40° C. for three days.

If any gas-forming bacteria be present, gas will collect in the closed limb of the tube, and some knowledge of the numbers of such organisms present may be gained by observing how many of the ten tubes show the reaction.

The amount of gas produced is stated in percentages of the length of the closed limb. *B. coli communis* will fill this closed limb about half full of gas, and will do so rapidly, usually ceasing to form any more after the end of the first day. Sundry other "gas-formers" act much more slowly. Therefore note the volume of gas formed during each of the three days.

The total gas will often on the third day be diminished in volume, due to solution of CO_2 in the liquid present.

To determine the CO_2, fill the bulb to overflowing with solution of KOH; close the orifice with the thumb and tilt the tube a number of times to cause the KOH to absorb the CO_2. The remaining gas is rated as hydrogen, although it contains also a little nitrogen and methane, as shown by Pennington and Küsel.

Sowings from pure cultures gave the following averages: Total gas, 35.3 per cent.; gas formed during first day (as percentage of total gas), 100 per cent.; ratio of H to CO_2, 71 to 29.

2. The liquid in the bulb of the fermentation tube must be distinctly acid to indicate *B. coli*.

3. *Indol* (C_8H_7N) is a compound belonging to the aromatic series, which produces a red color when acted upon by nitrous acid. It is formed by the breaking up of peptone by the action of putrefactive bacteria, including *B. coli*.

To test for its presence, place 25 c.c. of the water, together with 50 c.c. of sterile Dunham's solution, in a sterilized cotton-plugged flask, and keep the same in the incubator at 38° to 40° C. for three days. The high temperature will destroy common water bacteria, but will encourage the growth of the colon group.

Place 2 c.c. strong sulphuric acid and 2 c.c. of sodium nitrite solution in a 100-c.c. "Nessler" jar. Cool. Dilute with 50 c.c. water and then pour in the previously cooled incubated culture prepared above. A red coloration indicates indol, and is an additional evidence of the presence of *B. coli*.

4. Inoculate "nutrient gelatin" from the incubated culture obtained in 3. Let the plates develop as usual and observe if any of the *non-liquefying* colonies are *whitish*, with *irregular, leafy* outlines and showing lines more or less radial. Such characteristics point to *B. coli*.

5. Place a quantity of new milk in an Arnold's sterilizer for fifteen minutes, and afterward allow it to stand overnight in a cool place. Siphon off the lower layer of milk, avoiding the cream. Place it in cotton-plugged test tubes and sterilize as usual. Add to several of these

tubes 1 c.c. of the incubated culture obtained in 3, and keep in the dark at room temperature.

B. coli coagulates milk in from one to three days. Other forms usually take more time.

6. If inoculations from the colonies obtained in 4 be examined as "hanging-drop" cultures, the bacilli will be found to be motile if they be *B. coli*. This motility may be manifested, however, by only a portion of the bacilli present in the field, and its intensity will be far less than that shown by the typhoid bacillus.

7. Add 25 c.c. of the water to a flask of "nitrate solution" and place in the incubator for three days. Test the contents of the flask at the end of that time for "nitrite."

B. coli reduces the nitrate to nitrite.

A moment can be properly spent here upon the often broached topic of the recognition of the typhoid germ in water, and also a word added with reference to the diagnostic value of the demonstration of the presence of *Bacillus coli communis*.

Laws and Andrewes, in their report to the London County Council, show that the chance of discovering *B. typhosus* in sewage is exceedingly small. They entirely failed to find it in London sewage. Finally, they examined the sewage flowing (without disinfection) from the Eastern Hospital at Homeston, which same received the dejections of forty typhoid patients. Out of a whole series of samples examined from this latter source, only two colonies of *B. typhosus* were differentiated with certainty.

A similar experience has been recorded by practically all the recent observers, and consequently search for the typhoid germ in water is becoming very unusual.

The present position of this question is tersely summed up by Dr. W. H. Welch, of Johns Hopkins University: "The most which can be expected is the determination, not of the actual presence of the typhoid bacillus, but of the possibility or probability of its presence. Our principal guide at present in drawing conclusions as to the possible presence of the typhoid bacillus in suspected drinking-water is the recognition of fæcal bacteria, and more particularly of members of the colon group."

With regard to the diagnostic value of the colon group as supplying the much-needed "index of fæcal pollution," it must be stated that the group is widely distributed, and is often found in waters that a "sanitary survey" would unquestionably pronounce pure; but it cannot be denied that its persistent presence in large numbers is an indication of pollution that must not be overlooked; and, moreover, the proof of its absence serves materially to aid in formulating an opinion concerning the purity of a water.

It is, of course, possible to proceed much further than has been here outlined in the bacteriological examination of water, but for routine work it is doubtful if it pays to go beyond the tests already given. Moreover, it should be said that to make such tests of real value, they should be comparative in character; and the interpretation of results should be based upon data furnished by closely related local standards.

"Microscopical" examination of water has for its object the study of such suspended material, whether organized or not, as may be examined directly without the intervention of the "culture" methods required for bacteria. Plants and animals, dead or alive, amorphous organic material and inorganic particles of all kinds, are classified and their numbers estimated by this form of investigation. It is of especial value in determining the cause of those disagreeable odors and tastes which occur in stored water from the abundant growth of certain small aquatic plants. Concentration of the water sample is, of course, necessary in order to make a proper examination possible, and this end is accomplished by a modification of the original Sedgwick-Rafter apparatus.

This is a glass cylinder two inches in diameter, terminating in a conical base. The small cylindrical prolongation of the cone's apex is two and one-half inches long and one-half inch in diameter. A perforated rubber stopper, with its hole covered by a disc of fine bolting-cloth, is fitted to the smaller end of the funnel and about three-fourths inch of carefully screened fine sand (between eighty and one hundred mesh) is poured into the narrow tube and wet down with distilled water. From 250 to 500 c.c. of the water under examination are now permitted to filter through the sand. After the water has run through, the sand with the material strained off by it is washed into a test tube by 5 c.c. of distilled water delivered from a pipette. The organisms, sinking in the test tube much more slowly than the sand grains, may be decanted, with the water in which they float, into a second test tube. From this decanted portion, after agitation, 1 c.c. is delivered by a pipette to a covered "counting cell," which it completely fills. The objects discovered in this counting cell will, if multiplied by five, give the total number originally existing in the entire volume of water filtered.

It is manifestly impossible, in an article such as this, to dwell at length upon the very extensive subject of microscopic examination; therefore for purposes of general differentiation recourse must be had to the writings of biologists who have made such work a specialty.

William P. Mason.

WATER-GAS, POISONING BY.—Water gas is a mixture of carbon monoxide and hydrogen with some nitrogen and carbon dioxide, obtained by the action of steam on highly heated carbon (*e.g.*, coke or anthracite). It is nearly odorless and burns with non-luminous flame. For use as an illuminant, it is enriched; that is, charged with hydrocarbons from petroleum or bituminous coal. In this form it has come into extensive use. Owing to the highly poisonous character of carbon monoxide as compared with the hydrocarbons that form the bulk of the older "coal gas," a great increase in fatalities from the inhalation of illuminating gas has been noticed in the mortality statistics of late years. The characteristic effect of carbon monoxide is its affinity for hæmoglobin, with which it forms a compound that cannot be broken up by free oxygen. Hence, even a small amount of carbon monoxide in the inspired air will cause a steady accumulation of the toxic material until so much of the hæmoglobin is rendered inactive that death results from a chemical asphyxia. The symptoms are marked muscular weakness, rapid pulse, flushed face, and a strong tendency to sleep. The blood becomes abnormally red, the breathing becomes stertorous, and the patient dies from failure of respiration. If the patient be rescued before the condition is far advanced, the return to consciousness is slow, even under treatment, and a fatal result from brain disease may yet occur. In advanced cases, red spots are noted on the skin. The blood putrefies much more slowly than normal blood. The fatal period is somewhat uncertain, but may be several hours. The treatment is not satisfactory. Artificial respiration does little good. Inhalation of oxygen under pressure has been proposed, but this method does not promise much. Transfusion of blood has been successful in experiments on animals. Good results have been claimed for the administration, by the stomach and hypodermically, of hydrogen dioxide, but this seems doubtful. Hot applications should be used to restore normal temperature. The bright redness and slow putrefaction of the blood are important post-mortem data. Several chemical tests have been proposed, but they are not very satisfactory in actual practice, as ordinary illuminating gas contains several active substances.

Henry Leffmann.

WATSON'S SPRINGS.—Greene County, Georgia.

POST-OFFICE.—Maxey's boarding-houses and cottages.

These springs are located eleven miles north of Greensboro, on the Georgia Railroad, and eight miles west of Maxey's Depot, on the Athens branch of the Georgia Railroad. The group is one-quarter of a mile from the Oconee River, which will be navigable at this point when the government works on the river are completed.

The springs are reached by private conveyance from the points above mentioned. The scenery in the neighborhood of the springs is varied and the climate delightful, the temperature rarely falling below the freezing point in winter or rising above 90° F. in summer (95° F. is the highest temperature known). The springs are four in number, viz.: the "Sulphur" Spring, the "Chalybeate," the "Alum," and the "Ice" Spring. The following partial analysis of two of the springs was made some years ago by Dr. J. R. Duggan:

The Sulphur Spring contains calcium carbonate, potassium carbonate, iron carbonate, potassium sulphate, sodium sulphate, sodium chloride, silicic acid, hydrogen sulphide gas, and carbonic acid gas. The temperature of the water is 59° F.

The Chalybeate Spring contains iron carbonate, magnesium carbonate, sodium chloride, potassium sulphate, calcium sulphate, and silica. The temperature of the water is 61° F.

The "Ice" spring has not been analyzed, but its waters more than forty boarding-houses. In addition, the houses of private citizens are often thrown open to visitors. Among the best-known hotels are the Fountain Spring House, which accommodates 800 guests, the Park, 300; the Spring City, 250; National, 150; Terrace, 100, etc. Most of the hotels maintain bands during the season. Open-air public concerts are also given morning and evening. There is one theatre in the place besides two public halls. The Fox River runs through Waukesha, and is large enough for row boats. This is a region of lakes, there being no less than thirty-six in Waukesha County, the most remote being only eighteen miles distant. The lakes are surrounded by hotels and cottages, and during the summer they constitute a vast picnic ground. The prime attraction of Waukesha, however, is found in the great group of mineral springs located here. The waters of these springs are chiefly alkaline, chalybeate, and calcic. They have become known throughout the United States. Following are analyses of some of the most important:

ONE UNITED STATES GALLON CONTAINS:

Solids.	Bethesda. C. F. Chandler. Grains.	CLYSMIC			Fountain. Blaney. Grains.	Hygeia. A. Thiel. Grains.	Silurian. W. S. Haines. Grains.	Vesta. G. Bode. Grains.
		1. Rathbone. Grains.	2. R. O. Doremus. Grains.	3. R. O. Doremus. Grains.				
Sodium bicarbonate	1.26	1.26	4.31	0.80	1.02	2.36	0.30	0.41
Calcium carbonate	....	....	....	....	....	....	9.93	
Calcium bicarbonate	17.02	16.04	16.15	15.90	15.58	16.75	....	13.43
Magnesium carbonate	....	....	....	....	....	....	6.83	
Magnesium bicarbonate	12.39	13.56	9.22	8.54	9.20	13.14	....	10.74
Iron carbonate	....	....	....	....	....	....	.13	
Iron bicarbonate	.04	.04	.57	.69	.05	.58	....	.05
Iron phosphate	....	....	....	....	....	....	Trace	
Sodium sulphate	.54	.56	.69	1.08	.36	.52	.29	.55
Manganese phosphate	....	....	....	....	....	....	Trace	
Potassium sulphate	.46	.46	.50	.20	....	.82		
Sodium phosphate	....	.03	.43	.15	....	.04		
Sodium chloride	1.16	1.17	.35	.55	Trace	1.25	.19	0.30
Aluminum oxide	.12	Trace	....	....	.09	.72	59	.13
Alumina	....	....	Trace	Trace	....	....	....	
Silica	.54	.72	.80	.81	.85	.15	.70	.85
Organic matter	1.98	1.62	Trace	Trace	.31	Trace	Trace	
Total	35.71	35.46	33.02	29.02	25.36	36.21	18.69	26.46

are delightfully cold and refreshing and palatable at all times. The sulphur and chalybeate springs yield about one gallon of water per minute. Their waters are stated to be highly efficacious in rheumatism and dyspepsia, and in renal, cutaneous, and blood diseases.

James K. Crook.

WAUKESHA MINERAL SPRINGS.—Waukesha County, Wisconsin.

POST-OFFICE.—Waukesha. Hotels and boarding-houses.

ACCESS.—Viâ Chicago and Northwestern, Chicago, Milwaukee, and St. Paul, and Wisconsin Central Railroad. An electric line is also being built from Milwaukee.

Waukesha, the county seat of Waukesha County, is located sixteen miles west of Milwaukee, and ninety-eight miles northwest of Chicago. The elevation here is about 800 feet above tide-water. The surrounding country is of a rolling character, well wooded and has a sandy, gravelly soil. The natural advantages of the place have made it a general society centre of the Northwest during the summer season. The usual population, of about sixty-four hundred, is increased during the hot months to more than ten thousand. In the year 1895 there were one hundred and forty-three clear days, one hundred and thirty partially cloudy, and ninety-two cloudy days. The summer weather is usually of a delightful character, and quite free from days of oppressive heat. The average annual rainfall from 1892 to 1895, inclusive, was 28.02 inches. The village contains eleven hotels and

Other well-known springs at Waukesha are the "White Rock," "Glen," "Horeb," "Gibson," "Siloam," "Mineral Rock," and "Vitaqua." It will be observed that the principal ingredients of all these waters is the bicarbonate of magnesium. Their action in the system is antacid, mildly laxative after continuous use, and diuretic. They have a useful application in dyspepsia, abdominal engorgement, Bright's disease, diabetes, and bladder troubles. Some of them are excellently adapted for table use.

James K. Crook.

WAX; BEESWAX.—(*Cera Flava*, U. S. P., B. P., P. G.); A peculiar, concrete substance, prepared by *Apis mellifica* L. (Ord. *Hymenoptera*).

Wax is an animal product secreted by bees under the rings of the abdomen, where it accumulates, when the insects are comb-making, in scales or flakes. These flakes are disengaged by the bees, and, with jaws and legs, moulded into that remarkable structure, the honeycomb. It appears to be an analogue of the sebaceous secretion of the skin. The wax is obtained by depriving the comb of its honey by draining and pressing, and is purified by melting one or more times in boiling water and cooling. It is then melted and cast in large solid cakes.

Wax is too familiar to need description, were it not for its very frequent adulteration, which unfortunately is not always easily detected. The Pharmacopœial description and tests are as follows: "A yellowish or brownish-yellow solid, having an agreeable, honey-like odor, and a faint, balsamic taste. It is brittle when cold, but be-

comes plastic by the heat of the hand. It melts at 63–64° C. (145.4°–147.2° F.), and congeals with a smooth and level surface. Specific gravity, 0.955–0.967. It is insoluble in water, but soluble in 35 parts of ether and in 11 parts of chloroform; also soluble in the oil of turpentine and in fixed or volatile oils. Cold alcohol dissolves it only partly, but it is almost completely soluble in boiling alcohol." Boiled with a solution of soda, wax does not saponify like the fats and resins, and their mixture with wax can be detected in this way: if the liquid so boiled, after the wax has been separated by cooling, remains turbid, or gives a precipitate when acidulated with hydrochloric acid, fat, resin, soap, or something of that kind is present. "If 5 gm. of wax be heated, in a flask for fifteen minutes, with 25 gm. of sulphuric acid, to 160° C. (320° F.), and the mixture diluted with water, no solid, wax-like body should separate (absence of paraffin)."

The composition of wax is: *Cerin*, an ether of cerotic acid and ceryl alcohol, $\left.\begin{matrix}C_{27}H_{53}O\\C_{27}H_{53}\end{matrix}\right\}O$, ten per cent.; and *myricin*, an ether of palmitic acid and myricyl alcohol, $\left.\begin{matrix}C_{16}H_{31}O\\C_{30}H_{61}\end{matrix}\right\}O$, ninety per cent. ("Encyclopædia Britannica"), together with traces of coloring and aromatic substances. White wax (*Cera Alba*, U. S. P.) is yellow wax bleached, usually by being cut into thin ribbons or shreds and exposed for a few weeks to the atmosphere and sunlight, being also frequently watered. It may also be bleached by the less desirable method of treatment with the oil of turpentine or some chlorine solution. It is a yellowish-white solid, somewhat translucent in thin layers, having a slightly rancid odor and an insipid taste, answering otherwise nearly to the description and tests given above.

Action and Uses.—Wax is insoluble in the body, and therefore exerts only a mechanical action upon it. Its use internally is entirely obsolete. Formerly it was occasionally recommended for diarrhœa or dysentery, and later, as a pill-coating. Its plasticity and very great permanence make it useful as a temporary tooth-filling where the cavities are tender and away from the grinding surfaces. Its principal employment in medicine, however, is as a component of cerates (which derive their name from it), plasters, and ointments, to which it gives durability and consistence. It is perfectly unirritating.

The most important uses of wax are ceremonial and domestic—candles and mechanical moulding and modelling.

Allied Substances.—Chinese wax, secreted by Coccus ceriferus upon a Chinese ash; a hard, translucent, spermaceti-like substance; Japanese, from the surface of the fruits of several species of Rhus; bayberry wax and several other vegetable products. See also *Spermaceti*.

W. *P. Bolles.*

WAXY DEGENERATION. See *Amyloid*, and *Necrosis*.

WEIGHTS AND MEASURES.—Balances and measures of capacity are brought into constant use in chemistry, pharmacy, and medicine. Means for the accurate determination of values are indispensable to science, industry, and commerce, and the development of scientific metrology is a concomitant of advancing civilization.

Old Weights and Measures.—The expressions used in ancient writings to indicate size, or quantity, the oldest units of measure, and the origin of decimal arithmetic, all have reference to the human body and its members. Bulk was measured by armfuls, handfuls, pinches; linear measure was expressed in such terms as "the height of a man," the fathom, stride, forearm (cubit), foot, hand, palm, finger, thumb, nail; the oldest expressions of weight had reference to loads or burdens; and decimal arithmetic had its origin in the number of fingers on the human hand. Seeds were later used as standards of comparison for the determination of weight, and also for linear measure; the "karat" and the "grain" originated in this manner. When coins were introduced they were frequently employed as weights, and the intimate relations which weights and coins sustained to each other are shown by the use of the same words to designate units of weight and monetary units, as "drachma," "livre," "pound," "mark," etc.

Commercial intercourse between different countries helped to spread the various weights, measures, and money from one country to another; but in the absence of proper governmental regulation, and in consequence of national prejudices and conflicting interests, the systems and units suffered changes which created confusion. The same, or very similar, names were given to units of differing values, and different methods of subdivision increased the diversity. This chaotic condition of the weights and measures of the civilized world is sufficiently shown in the following tables:

Pounds and Grains Used at Various Times in Different Countries.

Country or locality.	Value of the pound in grains.	Number of grains in each pound.	Value of the grain in grains.
France ("livre métrique")	500.0	9,216	0.054
Germany ("zollpfund") [1]	500.0		
France ("livre poids de marc")	489.5		
England and the United States (avoirdupois pound)	453.59	7,000	.065–
Sweden [2]	425.0		
Austria	420.0	5,760	.073+
Netherlands and Switzerland	375.0	5,760	.065+
England and the United States (troy pound and apothecary's pound)	373.24+	5,760	.065–
Amsterdam	371.0		
Bavaria and Greece	360.0	5,760	.063–
Poland	358.5		
Russia	358.3	5,760	.062+
Norway	357.85–	5,760	.062+
"Nüremberg Pound" [3]	357.664–	5,760	.062+
Sweden	356.25–	5,760	.061–
Prussia	350.8	5,760	.061–
Spain	345.1	6,912	.050–
Portugal and Brazil	344.25		
Tuscany	339.5	6,912	.049+
Papal States	339.7		
Turin	322.0	6,912	.048+
Naples and Sicily	320.8	7,200	.045–
Sardinia	307.4	5,760	.053+
Venice	301.2	5,760	.052+
Mons	279.0		
Baden	214.25		

[1] Subdivided into 30,000 "korn."
[2] Subdivided into 10,000 "korn."
[3] Officially recognized by many pharmacopœias, among which were those of Nüremberg, Finland, Hamburg, Schleswig-Holstein, Russia (military pharmacopœia of 1840), Baden, Hanover, Hesse, Bremen, Lübeck, Nassau, etc.

The ounces, drachms, and scruples, of course, varied as much. The pound was generally subdivided into 12 ounces; but sometimes into 16; the ounce into 8 drachms, but one of them into 16; the scruple into 20 grains, but sometimes into 24.

Varying Value of the Foot.

	Value in millimetres.
Hesse (the Grand Duchy)	250
Saxony	283
Frankfurt a. M.	284
Brunswick	285
Württemberg and Hamburg	286
Hesse (Kur-Hessen)	287
Bavaria	291
Hanover	292
Sweden	297
Baden	300
England	305
Prussia (Rheinish)	313
Norway	314
Austria	316
Paris	324

In England alone there have been four different kinds of gallons, quarts, and pints.

Legislation relating to weights and measures aimed to fix the values of existing units so as to prevent variation

but not to establish new systems in accordance with recognized scientific principles, nor to secure any degree of international agreement. The following examples of early English laws will indicate their character: "An English penny, called a sterling, round, and without clipping, shall weigh thirty-two wheat corns from the midst of the ear, and twenty pence shall make an ounce, and twelve ounces one pound, and eight pounds do make a gallon of wine, and eight gallons of wine do make a London bushel, which is the eighth part of a quarter." (King Henry III., A.D. 1266.)

"Three barley corns, round and dry, shall make an inch, and twelve inches a foot." (Edward III., A.D. 1324.)

"We will and establish that one weight, one measure, and one yard be throughout the land, and that woollens and all manner of avoirdupois be weighed." (Edward III., A.D. 1353.)

PRINCIPLES OF METROLOGY.—All values, of whatever kind, are expressed by comparison with known standards. Matter may be measured, as to its amount, either by its weight or by its volume. Convenience and the desired degree of accuracy determine the choice of method. As by matter we understand the weighable, without regard to space, it follows that a given amount by weight of any substance is a constant quantity without regard to its volume; but a given volume of matter is a variable amount, because the mass occupies more or less space according to its density, temperature, and the pressure to which it is subject. Extension is, however, much more readily and strikingly perceptible to our physical senses than weight, and we can, moreover, think of space as well as of distance without regard to matter; while the idea of weight is inseparable from matter as well as space. Hence a rational system of weights, measures, and money ought to rest upon some fixed unit of linear measure as its basis.

Whatever may be the natural basis of the primary unit of linear measure, if the weights and measures have such a basis, all of the scales and measures used to measure linear extension, and all volume measures and weights must be derived from, or standardized by, comparison with actual *prototype standards*. The British weights and measures do not rest upon any physical constant, but upon the prototype yard and the prototype pound weights. The metric system, however, rests theoretically upon the length of the meridian, and practically upon the platinum rod which represents the theoretical metre, and upon the platinum weight which represents the theoretical kilogram. Distinction must be made between theoretical and actual standards. While the theoretical metre is the forty-millionth part of the length of the meridian, the actual metre, made of platinum, may not be absolutely one theoretical metre in length. The theoretical litre is the cube upon the tenth part of the metre, but the actual litre measure used in practical work may vary from it. The theoretical kilogram is the weight, *in vacuo*, of one cubic decimetre of pure water at 4° C., but the actual (prototype) platinum kilogram, made to represent that weight, may not be true. It will be easily understood, then, that the material standards or models are the real standards; that it is of the utmost importance that a sufficient number of perfect copies of these prototype standards be carefully preserved in different places; but that a knowledge of the exact relation of these prototypes to any geographical constant is of no consequence.

After fixed standards of linear measure have been adopted, the units for the expression of surface measures are furnished by the squares upon the linear units, and measures of capacity or bulk are derived from their cubes. Thus the unit of land measure of the metric system is the square of ten metres, called an ARE; the unit for measuring large bulks of dry substances is the cubic metre, called a STÈRE, and the unit of liquid and dry measure used for less bulky commodities, is the cube upon the tenth part of the metre, called a LITRE. Next in order comes the unit of weight, which is derived from the mass of a given volume of water, under such conditions as are most favorable to exact determinations.

Water has been chosen as the medium by which weight and volume are compared, and its density as the standard unit for the expression of specific weight, because it is universally present, easily obtainable in a pure state, and offers the most favorable conditions for conveniently and accurately determining the relations between its weight and its volume. In the construction of the metric system, therefore, the weight unit is derived from the weight, *in vacuo*, of one litre of pure water at its maximum density (the theoretical kilogram), which is represented by the prototype standard weight of platinum (the actual kilogram of the French Archives). The one-thousandth part of this mass, called a GRAM, is the principal weight-unit of the metric system. The monetary unit of the French, and of several other nations, represents the value of 5 gm. of silver of legal standard fineness, and thus the whole chain of standard units of measures, weights, and money is completed, and all of these units bear simple reciprocal relations.

A perfect system of metrology must also present units of such value as will best subserve the practical requirements of science, commerce, arts, and manufactures, and it should be in harmony with the arithmetical notation in use.

How far the metrological systems now in use accord with these simple principles, may be readily discovered by even a superficial examination.

ARITHMETIC AND METROLOGY.—The intimate relation of metrology to our arithmetical notation commands universal recognition. Whatever may be the periodical number of our arithmetical notation, that number should also be the periodical number governing the subdivision of the larger metrological units into the next lower. So long as whole numbers are expressed in units, tens, hundreds, and thousands, so must ten, or a hundred, or a thousand of the principal units of weight and measure make the higher secondary units, and the tenth parts, hundredth parts, and thousandth parts must furnish the lower secondary units, because this conformity reduces the labor of computations to its minimum. The main reason, then, why the metric system has become universally adopted for scientific purposes is that it agrees with our arithmetic; and many efforts have been made to impart a decimal character to old systems.

Whether or not the periodical number of our arithmetical notation is the most natural, simple, and useful is, however, questioned. It is admittedly derived from the fact that man has ten fingers, and that in its early childhood the human race needed and made use of this aid in counting, until finally the habit of counting upon the fingers and repeating that count, or counting by tens, became so rooted that it was made the basis of our arithmetical notation. But decimal arithmetic has nothing to recommend it except that it is in universal use. The fact that no other system is at all employed would, however, render a change extremely difficult, no matter how clearly it may be shown that some other system would be so far superior as to be well worth the great labor probably involved in its introduction. The most natural and convenient arithmetical processes are surely those in harmony with the constitution of man's mind, without regard to his fingers and toes. The most simple subdivision and method of counting is by twos, and although education and habit have for several centuries trained mankind in the use of a decimal arithmetical system, the question still continues to force itself upon our attention: Is not any arithmetic unnatural which is based upon a periodical number indivisible by both 3 and 4, and comprehending neither the square nor the cube of any number? Of course, the periodical number must not be too large nor too small, and we have found 10 to be manageable; two other numbers have been suggested as more simple and effective than 10, namely 8 and 12. The number 10 will be readily regarded as more suitable than 7, 11, or 13; but 8 and 12 are each as clearly superior to 10, as the periodical numbers of arithmetical nota-

tion as well as of weights, measures, and money. Notwithstanding the universal inclination of the untutored human mind to count upon the fingers and toes, and despite the universality of the decimal system of numeration as the result of that primitive instinct, mankind did not adopt decimal division and multiplication in regard to measurements of length, surface, volume, weight, money, or time; but the subdivisions and multiples adopted were by 2, 4, 8, 16, and 32, and by 3, 12, 24, and 60.

The number 12 has been recommended as a periodical number, because it is evenly divisible by 2, 3, 4, and 6; and 8 has been proposed, because, without being either too small or too large, it is the cube of 2, which is the smallest number above the unit; one-half of 8 is the square of 2, and three successive divisions by 2 gives 1 as the last quotient.

Octonary notation would, of course, be quite as easy as decimal notation, and more natural. It would require but eight figures including the cypher; two figures would be used to write eight, and three figures to write eight times eight, etc., and we would have an octonal point instead of the decimal point.

To show the most common subdivisions of weights and measures, the following will suffice:

Distance Measure: 1 mile = 8 furlongs. 1 furlong = 40 rods. But furlongs and rods are not so often mentioned as "half miles," "quarter miles," eighths of a mile, etc.

For shorter linear measures we find: 1 yard = 3 feet. 1 foot = 12 inches.

The yard is used most frequently in measuring cloth, but no one uses such expressions as "a yard and one foot or "a yard and one foot and six inches"; we would instead say "a yard and a third," or "a yard and a half." Halves, quarters, and eighths of a yard are more commonly referred to than any other fractions when the measure need not or cannot be exact, notwithstanding the subdivision of the yard into three feet or thirty-six inches. But the yard was derived from the length of the arm of King Henry I., in 1101; and it was divided into three feet, because the third of it was not very far from the length of a man's foot; and the subdivision of the foot into twelve inches was continued, because one-thirty-sixth of the yard was about the length of a man's thumb from the end to the first joint. In other words, these units were adopted for the sake of preserving the use of the valuable object lessons afforded by the members of the body, rather than to insure the most convenient and valuable mathematical results. Inches are subdivided into halves, fourths, eighths, sixteenths, and thirty-seconds, more frequently and naturally than into tenths. And yet the foot has, in some countries, been subdivided into ten inches instead of twelve, and each inch into ten lines instead of twelve, in obedience to the demand that the metrological subdivisions shall agree with the arithmetic.

Land Measure.

1 square mile = 640 acres.
1 acre = 4 roods.

But we speak commonly of half acres and quarter acres, and not of roods.

Volume Measure.

1 bushel	= 4 pecks or 8 gallons.
1 peck	= 2 gallons or 8 quarts.
1 gallon	= 4 quarts or 8 pints.
1 quart	= 2 pints or 8 gills.
1 pint	= 4 gills or 16 fluidounces.
1 gill	= 4 fluidounces or 32 fluidrachms.
1 fluidounce	= 8 fluidrachms.
1 fluidrachm	= 60 minims.

In these subdivisions there was nothing to prevent the consistent application of the natural inclination to divide the larger units into two, four, eight, sixteen, or thirty-two parts, until the fluidrachm was reached; but the fluidrachm was subdivided into sixty minims, because it was desired to make the subdivisions of the fluidounce, which was used only by physicians and apothecaries, parallel with the subdivisions of the ounce.

In the imperial pint there are twenty fluidounces instead of sixteen, as the unavoidable result of making the avoirdupois ounce commensurate with the fluidounce, while the gallon was made to represent the volume of ten pounds of water.

Avoirdupois Weight.

1 pound = 16 ounces.
1 ounce = 16 drachms or 437½ grains.

But the awkward subdivision of the ounce into 437.5 grains was simply the direct result of combining portions of two different systems, and avoirdupois weight did not originally include any smaller unit than the drachm. We no longer make use of the avoirdupois drachm, but do make use of halves, quarters, and eighths of the avoirdupois ounce, having weights of these denominations among the sets in common use in our shops.

Troy Weight.

1 pound	= 12 ounces, or 240 pennyweights.
1 ounce	= 20 pennyweights or 480 grains.
1 pennyweight	= 24 grains.

Old Medicinal Weights.

1 pound	= 12 ounces.
1 ounce	= 8 drachms or 24 scruples.
1 drachm	= 3 scruples or 60 grains.
1 scruple	= 20 grains.

Sometimes the scruple contained twenty-four grains.

From the above examples it will be seen that two principal considerations have determined the subdivision of the larger into smaller units, namely: (1) Capacity for continued integral bisection down to unit; and (2) divisibility by a variety of aliquot parts.

The Romans divided their acre, their foot, and their pound, each into twelfths (*unciæ*, from which our "ounce" and "inch"); the signs of the Zodiac, the division of the year into twelve months, and of the day into twelve hours, and the use of the "dozen" and the "gross" also show that the number twelve has, next to eight, been a favorite periodical number. The number sixty has also been much used, because divisible into a great variety of aliquot parts. In the division of the earth's longitude and latitude, and in the division of time, the number sixty has been found valuable.

But we find no subdivisions by ten in the old methods of dividing measures, weights, time, or money.

The following table forcibly illustrates the natural tendency to binary and quarternary subdivision, and at the same time the redundance of units, which is a common fault in the several systems of weights, measures, and money.

In Baden the weights at one time used were:

4 richttheilen	= 1 gränchen.
4 gränchen	= 1 gran.
4 granen	= 1 karat.
4 karate	= 1 pfennig.
4 pfennig	= 1 quentchen.
4 quentchen	= 1 loth.
2 lothe	= 1 unze.
4 unzen	= 1 vierling.
2 vierling	= 1 mark.
2 mark	= 1 pfund.

American Weights and Measures.—No civilized country has failed to enact complete and specific laws establishing standards for the weights and measures used by its people, except the United States of America. All other nations have laws enumerating the several units

which shall be used, establishing their relations to each other, fixing their respective values, and providing for the construction and proper preservation of prototypes or models by which the weights and measures intended for the use of the people shall be standardized. In the United States there is no law for the establishment of any weights or measures other than one declaring a certain copy of the British prototype troy pound to be the standard "conformably to which the coinage shall be regulated." The weights and measures in actual use throughout the United States are the avoirdupois weight of the present British "Imperial System;" the troy weight and apothecaries' weight, which was abolished in England by a law passed in 1824, to take effect January 1st, 1826; the English linear measures; and the wine measures and Winchester measures, abolished in England simultaneously with the abolition of the apothecaries' weights. No law now exists, in this or any other country, which directly fixes the value and subdivisions of the liquid measures, the dry measures, or the medicinal weights and measures used in the United States.

The only United States laws relating to weights and measures are these: "For the purpose of securing a due conformity in weight of the coins of the United States, the brass troy pound procured by the minister of the United States at London, in the year 1827, for the use of the Mint, and now in the custody of the Mint at Philadelphia, shall be the standard troy pound of the Mint of the United States, conformably to which the coinage thereof shall be regulated." (R. S., 3548.)

By the act of July 28th, 1866, it was enacted that "it shall be lawful throughout the United States of America to employ the weights and measures of the metric system; and no contract, or dealing, or pleading in any court shall be deemed invalid or liable to objection because the weights or measures expressed or referred to therein are weights or measures of the metric system." (R. S., 3569.)

Tables of equivalents, showing the relations of the metric weights and measures to those in common use, were also made part of the law of 1866. (R. S., 3570.) The legal equivalents may be said to fix indirectly the values of our mile, yard, foot, inch, acre, wine-gallon, bushel, peck, quart, gill, fluidounce, fluidrachm, avoirdupois pound, ounce, and grain, with reference to the units of the metric system; but the equivalents thus established, however sufficient for the purposes for which they are intended, are inconsistent as well as inexact; they do not suffice to establish the weights and measures which may be lawfully used; they do not fix the values and subdivisions of the units sanctioned by usage and in common law, except indirectly and partially.

On the day preceding the date of the executive approval of the act to render the use of the metric system permissive, Congress passed a joint resolution requiring the Secretary of the Treasury to furnish to each State of the United States "one set of the standard weights and measures of the metric system for the use of the States, respectively;" but we have no legalized standard metre and standard kilogram, any more than we have legalized prototype standards of the weights and measures in common use.

The *present ultimate standards* upon which all weights and measures employed in the United States are based are the American national prototype standards of the metre and the kilogram, made of irido-platinum, received by the American Government from the International Bureau of Weights and Measures (near Paris) in 1890, which are in the custody of the National Bureau of Standards at Washington.

The American *yard* is defined to be equal to $\frac{3,600}{3,937}$ metre; the American commercial *pound* is defined as being equal to $\frac{700,000,000}{1,543,235,639}$ kgm.; and the American liquid *gallon* is the volume of 3,785.434 gm. (58,418.144 grains) of water at the temperature of its maximum density, weighed *in vacuo*.

While the liquid gallon is designed to be a *volume* of 231 cubic inches, it is determined or adjusted *by weight* on the assumption that 252.892 grains of water, at its maximum density, weighed *in vacuo*, measures one cubic inch. This value is derived from the accepted equivalents of the metre in inches and of the kilogram in grains, coupled with the assumption that the mass of one cubic decimetre of water is identical with that of the actual standard kilogram.

Equivalents.

1 metre = 39.3700 inches.
1 yard = 0.914402 metre.

1 litre = 0.26417 liquid gallon.
1 gallon = 3.785434 litres.
1 fluidounce = 29.5737 millilitres.

1 kgm. = 2.20462 pounds, or to 15,432.35639 grains.

1 pound = 453.5924277 gm.
1 commercial ounce = 28.3495 gm.
1 medicinal ounce = 31.10348 gm.
1 grain = 64.7898 mgm

1 fluidounce of water weighs 29.5737 gm., or 456.392 grains.
1 medicinal ounce of water measures 31.10348 millilitres, or 504.829 minims.

British Weights and Measures Prior to 1826, and now Used in the United States.—The weights and measures in use in England, prior to 1826, were the following. They are the weights and measures in common use in the United States at this time, except the beer measures, which are no longer used anywhere.

Linear Measures.

1 league = 3 miles = 5,280 yards = 15,840 feet.
1 mile = 8 furlongs = 1,760 yards = 5,280 feet.
1 furlong = 10 chains = 40 poles, or perches, or rods = 220 yards = 660 feet.
1 chain = 4 poles, or perches, or rods = 22 yards = 66 feet.
1 pole, or perch, or rod = 5½ yards = 16½ feet.
1 yard = 3 feet = 36 inches.
1 foot = 12 inches.

Superficial Measures.

1 square mile = 640 acres.
1 acre = 4 roods = 10 square chains = 160 square poles = 4,840 square yards = 43,560 square feet.
1 rood = 40 square poles = 1,210 square yards = 10,890 square feet.
1 square pole = 30¼ square yards = 272¼ square feet.
1 square yard = 9 square feet.
1 square foot = 144 square inches.

Cubic Measures.

1 cubic yard = 27 cubic feet.
1 cubic foot = 1,728 cubic inches.

Dry or Winchester Measures.

1 bushel = 4 pecks = 32 quarts = 2,150.42 cubic inches.
1 peck = 2 gallons = 8 quarts = 537.6 cubic inches.
1 gallon = 4 quarts = 8 pints = 268.8 cubic inches.
1 quart = 2 pints = 67.2 cubic inches.
1 pint = 33.6 cubic inches.

Beer Measure.

1 hogshead = 2 barrels = 72 gallons.
1 barrel = 36 gallons.
1 gallon = 4 quarts = 8 pints = 282 cubic inches.
1 quart = 2 pints = 70.50 cubic inches.
1 pint = 35.25 cubic inches.

Wine Measure.

1 hogshead = 2 barrels = 63 gallons.
1 barrel = 31½ gallons
1 gallon = 4 quarts = 8 pints = 231 cubic inches.
1 quart = 2 pints = 57.75 cubic inches
1 pint = 4 gills = 28.875 cubic inches.
1 gill = 7.219 cubic inches.

Medicinal Fluid Measures.

1 gallon = 4 quarts = 8 pints = 128 fluidounces = 231 cubic inches.
1 quart = 2 pints = 32 fluidounces.
1 pint = 16 fluidounces = 128 fluidrachms.
1 fluidounce = 8 fluidrachms = 480 minims.
1 fluidrachm = 60 minims.

Measures of Weight for General Merchandise.

(Avoirdupois.)

1 ton = 20 hundredweight = 2,240 pounds.
1 hundredweight = 8 stones = 112 pounds.
1 stone = 14 pounds.
1 pound = 16 ounces = 7,000 grains.
1 ounce = 16 drachms = 437½ grains.
1 drachm = 27$\frac{11}{32}$ grains.

Measures of Weight for Precious Metals, Jewels, and Coin.

(Troy.)

1 pound = 12 ounces = 240 pennyweights = 5,760 grains.
1 ounce = 20 pennyweights = 480 grains.
1 pennyweight = 24 grains.

Measures of Weight for Medicines.

1 pound = 12 ounces = 5,760 grains.
1 ounce = 8 drachms = 24 scruples = 480 grains.
1 drachm = 3 scruples = 60 grains.
1 scruple = 20 grains.

The British Imperial System.—The English weights and measures were reconstructed in 1824, when a law was passed which went into effect January 1st, 1826, establishing the "Imperial System of Weights and Measures," which is at the present time still in force. It includes the linear measures previously employed and the avoirdupois pound, the value of which was defined to be $\frac{7000}{5760}$ of the old standard troy pound of brass made in 1758. The new feature of the Imperial system was the Imperial gallon and its subdivisions, the old corn, beer, wine, and medicinal measures being replaced by the

Imperial Measures of Capacity.

1 bushel = 4 pecks = 8 gallons [= 2,218.191 cubic inches].
1 peck = 2 gallons = 8 quarts [= 554.548 cubic inches].
1 gallon = 4 quarts = 8 pints [= 277.274 cubic inches].
1 quart = 2 pints [= 69.3185 cubic inches].
1 pint = 20 fluidounces [= 34.65925 cubic inches].
1 fluidounce = 8 fluidrachms [= 1.733 cubic inches].
1 fluidrachm = 60 minims.

One of the carefully constructed copies (made of bronze) of the former standard yardstick, which had been destroyed, was declared to be the new standard, and a new avoirdupois pound-weight of platinum was made under the supervision of Prof. W. H. Miller, which, by the law of 1855, was declared to be "the legal and genuine standard measure of weight, and shall be, and be denominated, the Imperial Standard Pound Avoirdupois, and shall be deemed to be the only standard measure of weight from which all other weights and other measures having reference to weight shall be derived, computed, and ascertained; and one equal seven-thousandth part of such pound avoirdupois shall be a grain, and five thousand seven hundred and sixty such grains shall be, and be deemed to be, a pound troy. If, at any time hereafter, the said Imperial Standard Pound Avoirdupois be lost or in any manner destroyed, defaced, or otherwise injured, the Commissioners of Her Majesty's Treasury may cause the same to be restored by reference to, or adoption of, any of the copies," provided and available for that purpose.

Thus the avoirdupois pound, which was before based upon the troy pound-weight, became, in 1855, the only basis for all weights, including the troy weight, and also became the basis for the imperial gallon, which was defined to be the volume of ten avoirdupois pounds of pure water at 62° F.

Decimal Weights and Measures.—The first scientific decimal system of weights and measures ever presented was of American origin, being devised and recommended to the House of Representatives of the United States, July 13th, 1790, by Thomas Jefferson, who was then Secretary of State. Mr. Jefferson had been the American Minister to Paris, where he resided during the period of the great Revolution. He had, therefore, come into direct intercourse with the Bishop of Autun and other great men, who were inspired with the grand idea of establishing a common language of weights, measures, and money for the whole world. Mr. Jefferson proposed as a basis for his new system the length of a rod swinging seconds of time in latitude 45°, one-fifth of that length to be called the new foot. This new foot was about one-fourth inch shorter than the English foot. It was to be divided into ten inches, each inch into ten lines, and each line into ten points; ten feet was to be called a decade, ten decades a rood, ten roods a furlong, and ten furlongs a mile. A new cubic foot was to be the new bushel, the weight of the new cubic inch of water was to be the new ounce, and one ounce of silver $\frac{1}{15}$ fine was to be the new dollar.

Thomas Jefferson's decimal system of weights and measures was in every way as meritorious as the metric system, but it was not adopted. Other decimal systems have been proposed at various times, but none has been used except—

The Metric System.—A new system of weights and measures was constructed in 1791, with the view of its ultimate universal adoption. It was not the work of one mind. It was the legitimate offspring of the times. In its conception and development, as in its steadily increasing domain, no nation can claim it as its own.

Its basis was the length of the earth's circumference through the poles. The Dutch astronomer, Huygens, had already, in 1685, recommended the length of the meridian as a suitable standard for measures of length. The distance from the equator to the pole having been measured along the surface of still water, one ten-millionth part of that length was denominated a metre, and a platinum rod was made by Borda to represent the metre. The *theoretical metre* is one forty-millionth part of the length of the terrestrial meridian, and the *actual metre* is the distance between the ends of Borda's platinum rod at 0° C. They are generally supposed to be identical, but some physicists deny this. Be that as it may, the real basis of the metric system is the prototype platinum metre and not the length of the meridian; but this does not detract from the merits of that grand system. The value of the metric system depends upon the following characterisics: (1) Its construction is in perfect harmony with our present arithmetical notation, the multiples and subdivisions of all its units being in decimal progression. (2) The units of length, surface, capacity, and weight, all bear simple relations to each other, respectively, all being derived from the same primary standard, the metre. (3) Each volume unit of the metric system has a corresponding weight unit with which it is commensurate when referring to water, which is the connecting link between measures of extension and measures of weight, and the standard unit used for the expression of specific weight. Thus the units of weight and volume of the metric system are not merely parallel, but their values are readily interconvertible through the

specific weights and specific volumes of the substances measured or weighed.

The word "metre" is derived from the Greek, *μέτρον*, measure, and the term "metric system" from the metre.

There are only five standard units of the metric system. These are:

The *metre*, for linear measure; the *are*, for land measure; the *stère*, for large bulks; the *litre*, for smaller bulks; the *gram*, for weights.

The *are* is the square of ten metres, or a square dekametre.

The *stère* is the cube upon one metre, or a cubic metre.

The *litre* is the cube upon one-tenth of a metre, or a cubic decimetre. But, as all capacity measures are in reality made or adjusted by means of weighing, the actual litre is the volume of one kilogram of water at 4 C. in vacuo.

The *gram* is the weight of one one-thousandth part of one litre (1 c.c.) of water at 4° C. (39.2° F.) *in vacuo*.

Secondary and additional units are obtained by decimal multiplication or division, and the names of these subordinate units are constructed by the use of certain Greek and Latin numerals in the form of prefixes. These prefixes are as follows:

Myria-, meaning ten thousand.
Kilo-, meaning one thousand.
Hekto-, meaning one hundred.
Deka-, meaning ten; and
Deci, meaning one-tenth.
Centi-, meaning one one-hundredth.
Milli-, meaning one one-thousandth.

Of these prefixes, only two are very much employed—namely, "kilo-" and "milli-." The prefix "centi-" is also used to some extent; the rest of the prefixes are not only as superfluous as the "eagle," the "dime," and the "mill" in American money, but they burden the metric system.

"Kilometre" means a one-thousand-metre, or one thousand metres; kilogram is one thousand grams; 0.005 gm. is 5 mgm.; a centimetre is $\frac{1}{100}$ metre, etc.

It is more convenient to say "ten metres" than to say "one dekametre," but less convenient to say "one one-thousandth of a gram" than to say "one milligram." The choice of expression is, therefore, to some extent governed by euphony and convenience. But there is a redundance of units in the metric system which has doubtless retarded its introduction.

The orthography and pronunciation of the metric units are modified in each country according to the language of the people. In France the spelling and pronunciation are, of course, French, as mètre, litre, and gramme; in Germany they are German, being meter, liter, and gramm; in English-speaking countries and in Sweden we say and write metre, litre, and gram; Spaniards write gramo, and Russians gramma; etc. In our country the word centimetre should not be pronounced *sangtimátre* any more than cent should be pronounced *sangt*, or the word gas metre *gas-mátre*.

In abbreviating the metric terms there is unfortunately no uniformity of practice. The United States Pharmacopœia has adopted C.c. for cubic centimetre and Gm. for gram, and these are convenient and safe.

The metric system presents the following tables of measures and weights:

Linear Measures.

1 Myriametre	= 10,000		metres.
1 Kilometre	= 1,000		"
1 Hektometre	= 100		"
1 Dekametre	= 10		"
1 METRE	= 1		metre.
1 Decimetre	=	.1	"
1 Centimetre	=	.01	"
1 Millimetre	=	.001	"

In addition to the above units microscopists employ the "micro-millimetre," which is 0.001 millimetre.

Volume Measures.

1 Kilolitre	= 1,000		litres.
1 Hektolitre	= 100		"
1 Dekalitre	= 10		"
1 LITRE	= 1		litre.
1 Decilitre	=	.1	"
1 Centilitre	=	.01	"
1 Millilitre	=	.001	"

The only volume units employed by chemists, pharmacists, and physicians are the litre and the cubic centimetre. The cubic centimetre is practically identical with the millilitre.

Weights.

1 Kilogram	= 1,000		grams.
1 Hektogram	= 100		"
1 Dekagram	= 10		"
1 GRAM	= 1		gram.
1 Decigram	=	.1	"
1 Centigram	=	.01	"
1 Milligram	=	.001	"

In medicine and pharmacy the gram and the cubic centimetre are the most important metric units, and to express their close relationship the cubic centimetre has been very appropriately termed a "fluigram." The milligram is also indispensable.

COMPROMISE SYSTEMS.—Admiration for the metric system and its evident practical superiority were not sufficient to insure its rapid introduction. The old systems, however awkward and unscientific, were not to be displaced except under compulsion. In countries where legislation is the expression of the popular will the metric system has not yet been adopted for general use, nor was it easy to introduce it in any country. The prejudice against the foreign sound of the terms applied to the metric units proved so strong an obstacle that in some countries new names were invented, as in Italy and Greece, and even the names of old units were applied to the new values which the metric units represented.

In France, where the new system was first introduced by law, there were afterward compromises made between the old and the new weights and measures.

Various attempts were made in different countries to establish simple relations between the units of the old systems of weights and measures and the metric units, especially the weight units. The old systems were also changed so as to connect units of the same kind by decimal multiplication and division.

The German "Zoll-Pfund" was made equal to 500 gm. It was divided into 30 "loth"; but the loth was divided into 10 "quentchen," the quent into 10 "cents," and the cent into 10 "korn." Bremen and Hamburg had the Zoll-Pfund divided into tenths, hundredths, and thousandths, called "Unzen," "Neuloth," "Quinten," and "Halbgrammen." Sweden had a pound equal to 425 gm. and divided it into 100 "ort," each ort being subdivided into 100 "korn." Thus the Swedish korn differed greatly from the Prussian korn, and the quint of Bremen and Hamburg was 5 gm., while the quent of Prussia was but 1⅔ gm.

Decimal systems of linear measure were also devised and used.

But these compromise systems had none of the merits of the metric system, except their partly decimal character; no simple relations existed between the units of linear measure, the units of capacity, and the units of weight, respectively. Hence they were short-lived.

SUITABLE UNITS.—The number and size of the units of weight and measure are important considerations. There are often too many units of each kind of measure. Baden at one time had fifteen different weight units. In order to have convenient units for all ordinary purposes, it is not necessary that they should be near each other in value as they are in the metric system; instead of making a new unit for every multiplication by ten, it would be

sufficient to make one for each multiplication by one hundred, or even one thousand.

Each branch of science, trade, or business, will use the units best adapted to its particular purposes; but there is a superabundance of middle terms.

For certain special purposes, however, the smallest units we have are too large; thus it has been necessary to add a new metric unit of length for microscopical measurements (the micromillimetre); the grain is much too large as the smallest unit of weight for medicinal purposes and in analytical chemistry, the milligram being far more suitable; the cubic centimetre is too large as the smallest unit of volume in medicine, where the minim is greatly to be preferred.

Experience has shown that the use of decimal fractions is a source of frequent errors, and that in the practice of medicine and pharmacy the decimal point is dangerous, not only from want of familiarity with its right use, but chiefly because it is so often illegible, or accidentally misplaced, omitted, or duplicated. This undeniable fact must not, however, be regarded as an insurmountable obstacle to the use of the decimal *system* of weights and measures in medicine and pharmacy, but simply as an argument against the use of the decimal *point*. Use the smallest units and write whole numbers instead of fractions. In constructing prescriptions it is better to write "15 milligrams" than to write "0.015 Gm."

No decimal fractions were formerly used in writing prescriptions, because the grain was a small enough unit so long as alkaloids and other extremely potent remedies were unknown; and later, whenever the quantity required was less than a grain, *common fractions* were used to express it.

Weighing and Measuring.—When the greatest possible accuracy is required, as in some of the operations of physicists and chemists, matter is measured as to its amount by weight rather than by volume, because a given weight of any substance always expresses the same amount without regard to temperature, and because volumes cannot be easily measured with great exactness. In laboratory work, weighing is generally both convenient and accurate; but volumetric analysis is also convenient, and affords correct results.

Medicines are either solid or liquid. The liquid medicines are necessarily taken or administered in doses by measure. Hence they should also be prescribed by measure, and that is the uniform practice in the English-speaking countries. This practice is consistent, accurate, and convenient. In other countries, however, the liquid medicines are prescribed by weight, although the doses can, of course, not be apportioned otherwise than by measure. This is not only inconsistent, but gives very inaccurate results, for the prescriber cannot express definite volumes by weight, nor can he calculate the volume of a mixture composed by weight.

The practice of prescribing, dispensing, and administering liquid medicine by volume is dictated by common sense, and its results are the most accurate that can be obtained.

Many advocates of the metric system seem to labor under the mistaken idea that metric prescriptions cannot or ought not to be written, except exclusively by weight; and, on the other hand, a number of those who do write prescriptions expressing all quantities in grams, actually intend that the liquids so prescribed shall be measured, writing grams when they really mean as many cubic centimetres, overlooking or ignoring the different densities of different liquids.

Specific Weight and Specific Volume.—The relation of the weight of a mass to its volume is called its specific weight; the specific weights of solids and liquids are expressed in water units, and of gases in hydrogen units. Thus, the specific weight of water being 1,000, the specific weight of any solid or liquid is found by dividing the weight of a given volume of it by the weight of the same volume of water. Specific weight is commonly, though inaccurately, called "specific gravity," and the number used to express the specific gravity of a solid or liquid, is that number which expresses how many times the weight of that liquid contains the weight of an equal volume of water. The specific weight of ether is called 0.750, because it weighs 0.750 times as much as an equal volume of water weighs. This mode of expression is the most convenient form in which the relative weights of equal volumes of various solids and liquids can be stated and compared.

To physicians and pharmacists, the reciprocal relations of weight and volume are of great practical importance. The abolition of the use of measures of capacity in the pharmacopœial formulas for tinctures, syrups, and other liquid preparations, in the last revision, further increases the importance of the subject. It has become especially desirable to have some convenient means of expressing and comparing the relative volumes of equal weights of different liquids, and of computing readily the volume of any definite amount by weight. For this purpose the writer of this article proposed, in 1883,* to use the term "specific volume" to designate the comparative volumes of liquids, and to express their specific volumes in the same manner as their specific weights are expressed, namely, in water units. Thus the specific volume of ether is 1.333, because a given quantity by weight of ether is 1.333 times as bulky as an equal quantity by weight of water. The specific volume of any substance is obtained by dividing one by its specific weight.

$$\frac{1}{\text{sp. w.}} = \text{sp. vol.}$$

To find the volume of any number of grams of any liquid, multiply by the specific volume; the product is the answer expressed in cubic centimetres.

The utility of a table of specific volumes will be readily appreciated, and such a table should be contained in the Pharmacopœia.

As the volume of any substance is affected by heat, the specific weights and specific volumes must be ascertained and expressed at definite temperatures. The water generally taken as a standard or unit of comparison is water at 4° C. (39.2° F.), at which temperature it reaches its maximum density; but many of the pycnometers, hydrometers, and other instruments used for taking specific weight, are adjusted with reference to water at 15° C. or at 15.6° C. as unit. At the same time, the standard temperature at which specific weights are taken, and to which our "tables of specific gravities" refer, is usually 15° C., but sometimes 15.56° C., 16.67° C., 14° C., and other temperatures. This is confusing. The standard temperatures to which our instruments are adjusted, the temperature which a liquid is assumed to have when its specific weight is taken, or at which it has the specific weight given for it, and the temperature of the water referred to as unit—all should be the same temperature. The writer has recommended for this purpose the temperature of 22° C. (71.6° F.), because that is slightly above the common room temperature at which we do our work, and therefore most convenient, as well as most useful and real under ordinary conditions.

Every volume unit of the metric system has a parallel weight unit, with which it is commensurate when referring to water. Thus:

1 litre of water weighs 1 kilogram.
1 decilitre of water weighs 1 hektogram.
1 centilitre of water weighs 1 dekagram.
1 millilitre of water weighs 1 gram.

This close relationship between the units of weight and of volume is of the greatest practical value. It enables us to find the weight of any volume of any liquid by simply multiplying the volume units by the specific weight, or to find the volume of any given weight of any liquid, by multiplying the weight units by the specific volume. The weight of one litre of any liquid, expressed in kilograms (or the weight of 1 c.c. expressed in grams), is the number expressing its specific weight. The vol-

* See Proceedings of the American Pharmaceutical Association, 1883.

ume of 1 kgm. of any liquid, expressed in litres, or the volume of 1 gm. expressed in cubic centimetres, is the number expressing its specific volume. Conversely, the number which expresses the specific weight is the weight of one litre in kilograms (or the weight of 1 c.c. in grams), and the number which expresses the specific volume is the volume of 1 kgm. expressed in litres, or of 1 gm. in cubic centimetres.

Commensurate units of weight and volume do not exist in any other system of weights and measures except the metric system and the British Imperial system. The British Imperial system, however, has only one pair of commensurate units—the fluidounce and the ounce—one fluidounce of water at 62° F. weighing one avoirdupois ounce. But it happens that six winepints of water at 60° F. weigh 100.0032 avoirdupois ounces, or only 1.4 grains more than 100 avoirdupois ounces, and hence we can most readily find the weight in avoirdupois ounces of six winepints or 96 United States apothecaries' fluidounces of any liquid, by multiplying its specific weight by one hundred, the answer being sufficiently accurate for nearly all purposes.

Weights and Measures in Prescriptions.—In writing prescriptions all solid substances are prescribed by weight, and all liquids by measure, and when solids and liquids are combined to form a liquid product, it is best, because most accurate, to adjust the total quantity to some definite volume. Thus, if a solution be prescribed containing corrosive chloride of mercury, potassium iodide, syrup, and water, it is, of course, impracticable for the prescriber to predict or calculate what will be the volume of the finished solution if he prescribes a given amount by weight or volume of the syrup and water; the only correct method in such a case is to prescribe water "q.s." to make a stated volume of finished solution.

When the old system of weights and measures is used, the most useful weight units are the grain and the ounce; but the drachm is also convenient and very much used. The scruple ought not to be used, because the sign employed to indicate it looks too nearly like the sign for the drachm. There ought to be a new unit of weight smaller than the grain, for prescribing and stating the doses of remedies intended to be administered in minute quantities, the new unit to be about gr. $\frac{1}{64}$, which is about 1 mgm. The units of capacity are the fluidounce, the fluidrachm, and the minim.

In writing prescriptions in which the quantities are expressed in units of the old system, these units are represented by certain universally recognized signs or abbreviations; the abbreviation "gr." (which should always be written with a *small* initial) denotes grain or grains; "ʒ" denotes drachm or drachms; "ℨ" denotes ounce or ounces; "℈" denotes scruple or scruples; "♏" denotes minim or minims; "f ʒ" denotes fluidrachm or fluidrachms; and "f ℨ" denotes fluidounce or fluidounces. The quantities directed to be taken are here to be indicated by *Roman* numerals, always placed *after* the signs or abbreviations, as follows: gr. x.; ʒ ij.; ℨ ss.; ℈ ij.; ♏ ix.; f ʒ iij.; f ℨ xij. The sign "ss." is used to express one-half, being an abbreviation of the Latin word *semis*.

When the metric units are employed in writing a prescription, it would save human lives to abstain from using the decimal point, and to use no other units but the gram and milligram for weights, and the fluigram or cubic centimetre for measures. The gram is abbreviated to "Gm," a *capital* initial always being used; the milligram should be abbreviated to mGm; and the fluigram to fGm (or the cubic centimetre, which is the same as a fluigram, to C.c.). The numerals indicating the number of weight units or volume units to be taken, should be always placed *before* the signs or abbreviations representing the units, and in writing them the *common* (or Arabic) numerals should be used, thus: 10 Gm.; 50 mGm.; 30 fGm. (or 30 C.c.).

When quantities expressed in units of one system are to be transposed into their corresponding equivalents in units of the other system, the following equivalents are sufficiently accurate and the most useful:

$\frac{1}{64}$ grain is equal to 1 mGm.
1 grain " " 64 mGm.
1 drachm " " 4 Gm.
1 ounce " " 32 Gm.

1 Gm. is equal to 16 grains.

1 minim is equal to $\frac{1}{16}$ fGm.
1 fluidrachm " 4 fGm.
1 fluidounce " 32 fGm.

1 fGm. is equal to 16 minims.

For further information concerning weights and measures, the reader is referred to the "Manual of Weights and Measures" by the writer of this article; Lowis A. Jackson's Work (London); "The Metric System," by F. A. P. Barnard; the Reports of Thomas Jefferson ("Works of Thomas Jefferson," vol. vii., pp. 472–495) and John Quincy Adams (Washington, 1821); the paper of Alfred B. Taylor on "Octonary Numeration and Its Application to a System of Weights and Measures," read before the American Philosophical Society, October 21st, 1887; and the Report of the Committee on Coinage, Weights, and Measures of the House of Representatives, January 7th, 1879 (45th Congress, 3d Session, H. R. Report, No. 53).

Oscar Oldberg

WEIL'S DISEASE.—An acute infectious (?) disease characterized by sudden onset with severe symptoms, prostration, a typical temperature, early-occurring jaundice, enlargement of liver and spleen, gastro-intestinal disturbances, and nephritis.

Though first described by Weil in 1886, and taken by him from amongst the diseases characterized by and associated with jaundice, the disease had been previously noted and described under various names: "Typhus hépatique bénin," "bilious typhoid," etc. After his first description it was seen that the disease had prevailed and was prevailing sporadically and not infrequently in the countries of Europe. No distinct descriptions of its occurrence in America are met with. There seems no doubt at present that the affection is distinct from such infections as typhoid, yellow fever, recurrent fever, diseases with which it was frequently confounded; its differentiation from acute yellow atrophy, simple infectious jaundice, and various intoxications is not so clear. Accurate post-mortem reports are few, owing to the benign character of the disease. Recent bacteriological investigations are not convincing.

Etiology.—Incidence of season, sex, age, and occupation. The majority of cases are met with in the warm months of the year, June to September. Ninety per cent. of those affected are men, usually at about the age of twenty-five to thirty years (third decade). Butchers, meat handlers, sewer and drain workers seem especially prone to infection. Outbreaks in garrisons and prisons occur not infrequently.

Specific Cause.—Although recognized by many as a morbid entity, and though a seemingly definite infection or intoxication, the question as to the specific cause of the disease is most unsettled. The abrupt onset without prodromal symptoms, the occurrence of some cases within a few hours of the ingestion of noxious material, sewer gas, sewage, tainted foods, etc., before bacteria could possibly have developed sufficiently to cause an infection, suggest strongly a ptomaïn poisoning or intoxication. One very typical case followed an overdose of santonin.

The febrile course; the peculiar febrile relapse occasionally seen; the inflammatory complications described in some instances—iridocyclitis, parotitis, adenitis, pleuritis, pneumonia—are more suggestive of a bacterial or infectious agent.

Infection is evidently through the alimentary canal, although it is not easy in some epidemics to exclude the possibility of entrance through the respiratory tract; the

present-day theory, however, of insect transportation of infectious material is readily applicable in this connection. The occurrence of several cases at any one time is probably due to exposure of all to the same infecting agent, rather than to infection of man from man. The frequent reports of epidemics among residents of garrisons and prisons after bathing in contaminated streams, after working in privies and sewers, or after living in unhygienic surroundings, seem confirmative of this idea.

Jaeger, Conradi, Vogt, *et al.*, have isolated a variety of proteus bacillus (B. proteus flavescens) from the urine and stools of four cases. No positive results have been obtained from the very few blood cultures made so far, and one must hesitate to accept the idea of a proteus infection being the constant cause. As in pneumonia, meningitis, and other infections there may be a variety of organisms capable of producing similar changes and symptoms. A variety of toxins or ptomaïns may, like phosphorus, exert a special influence upon the liver substance.

It is possible that the infecting substance enters the biliary system and liver directly from the intestine, being helped on its way by violent intestinal contraction. Further irritation by pancreatic secretion is a possibility under these conditions. In view of the fact that the symptoms appear simultaneously, it seems more probable that the infection starts from the intestines and is generalized by the blood. The relapse, as probably is the case in typhoid, may be due to reinfection from the gall-bladder.

Pathological Anatomy.—We have no recent descriptions of the post-mortem findings. The disease is rarely fatal. Auffrecht designated his cases as "acute parenchymatous disease," finding only "granular degeneration and cloudy swelling of cells of liver, kidney, and spleen." Acute gastro-enteritis, acute nephritis, splenic hypertrophy with inflammatory infiltration, advanced destructive changes in the liver, with fatty and leucocytic infiltration, proliferation of bile capillaries resembling the early changes in acute yellow atrophy, are described. The larger bile ducts are patulous. Obstruction is due to desquamative products obstructing smaller vessels. Inflammatory lesions in other organs present nothing distinctive.

Symptoms.—*General Description.*—Few diseases present a more typical course. The close similarity in all descriptions is striking. Later observers do not agree with Weil in considering the relapse or recrudescence of symptoms frequently seen a necessary characteristic. No prodromal symptoms are recorded or seem to exist. The suddenness of onset is one of the most important features of the disease. The majority of collected cases give a history of sudden collapse, while the patient is at work or on duty in apparent good health. A chill is frequent, severe headache, unconsciousness, delirium, prostration, vomiting, diarrhœa, abdominal pain are all present at the onset. Severe pain in the muscles of the legs is an almost constant symptom. Fever probably exists from the first, reaching 103°–105° F. By the second day all symptoms are exaggerated; by the third or fourth day jaundice, more or less intense, is already present; enlargement of liver and spleen, and albuminuria have appeared. The fever remains high, with slight morning remissions. The disease is at its height by the third or fourth day. From the fifth to the eighth day improvement takes place, the temperature falling by lysis, the hepatic and splenic enlargement diminishes, the albumin in the urine becomes quickly less, the nervous and other symptoms rapidly disappear. In Weil's four cases, after a fever-free interval of from one to seven days, a recrudescence of fever, lasting five or six days, took place, the other symptoms not, however, returning. As mentioned above, other observers do not consider this recrudescence an absolute characteristic of the disease. Convalescence is slow, lasting for from four to ten weeks. Traces of jaundice remain for days or weeks after the acute symptoms have subsided.

Analysis of Symptoms.—Complications.—Onset: The characteristic suddenness of onset is practically never missed. The majority of those affected are in bed by the second day of illness.

Temperature: The rapid rise has been noted. Occasionally a distinct fall takes place on the second day, only to be followed by an immediate rise to the maximum temperature, which is usually observed between the second and fourth days. A morning remission is early seen. The average duration of fever is from six to ten days, the fall to normal taking place by lysis; 106° F. may be given as the maximum, 103° F. as the average temperature. In thirty-seven per cent. of cases the recrudescence, or, better, relapse, is observed. Unlike the fever of onset that of the relapse is characterized by a gradual rise, rarely reaching the height of the first. The most common time of the relapse is from one to eight days after normal temperature has been reached. Cases with relapses as late as from the eleventh to the fourteenth day of apyrexia have been observed. The average duration of the relapse is five or six days.

Jaundice: Jaundice is of course always present. It is rarely seen before the second day, and is as a rule distinct by the third or the fifth day. It is usually well marked, but rarely as intense as in marked cases of obstructive jaundice. By from the ninth to the thirteenth day it may have disappeared. Traces persist, however, for several weeks. Increase of the jaundice during the relapse is rare. Bile-stained urine, colorless fæces are seen in the first few days, but as the obstruction of the bile flow is not complete and not in the main ducts, these characteristics are not extreme or long persistent. Itching is rather infrequent.

Condition of Liver, Spleen, and Kidneys: A recognizable enlargement of the liver is *not* a constant feature; it probably occurs in fifty per cent. of cases. When present it appears with the jaundice, usually at the fourth day. Reduction in size takes place with the lytic course of the fever. Re-enlargement during relapse is distinctly uncommon. Tenderness of the swollen liver is often noted.

In seventy-five per cent. of cases the spleen is noticeably enlarged, and can be readily palpated by the fourth day. The growth of the splenic tumor is rapid. Its shrinkage with the fall of fever is equally quick. Re-enlargement with relapse is more common than is the case with the liver. Marked albuminuria (acute nephritis) is present in about fifty-two per cent. of cases. The albumin is often excessive. Oliguria is a regular, anuria an occasional condition. Œdema is recorded but once in the cases collected. Casts and red blood cells are present in abundance. Bile reaction is marked. Distinct symptoms of uræmia are unusual. The renal condition clears up rapidly with the disappearance of the other symptoms. It may reappear with relapse. Traces of albumin, etc., can always be detected in the remaining percentage of cases. A polyuria during convalescence is usual. Hemorrhage from the bladder has been observed.

The gastro-intestinal tract is always disturbed. Vomiting is a frequent early symptom; diarrhœa an almost constant one. Distinct gastro-enteritis probably always occurs. Bloody stools are recorded. Symptoms of gastro-enteric disturbance quickly subside, and do not reappear with a relapse. The color of the stools has been noted.

The pulse keeps pace with the fever in the early days. Distinct slowing of heart's action takes place as apyrexia is approached. Endocardial murmurs are mentioned. The nervous symptoms described are those common to severe infections: delirium, convulsions, jactitations; they may outlast the fever, but are not observed in the relapse. Peripheral neuritis, hemiplegia, ophthalmoplegia have been seen toward the end of the acute symptoms.

Pains in the calves of the legs, present in half of the cases, may be neurotic or neuromuscular.

Intense prostration and slowness of convalescence are characteristic features of the disease.

Iridocyclitis as a late complication has been twice observed; retinal hemorrhage once.

Parotitis is a more frequent complication. In one instance it was double and suppurative.

Pneumonia and bronchopneumonia occur; a bronchitis at the onset is quite frequently seen. Pleurisy and pericarditis have been found in one fatal case.

Bleeding from the nose, apparently as a late symptom, seems a not unusual event.

In addition to the jaundice the skin in many instances has shown macular roseola-like rashes and petechiæ. Herpes labialis is an occasional feature.

Diagnosis.—The disease is no longer confused with yellow fever, recurrent fever, or malaria. It is evidently distinct from typhoid fever. Abortive typhoid fever, as some have classed the disease, never shows the severe regular symptoms of Weil's disease. Early jaundice in typhoid fever is rare, and then only in severe cases. The Widal reaction may be utilized as a means of confirming the diagnosis. Many of the reported cases give a history of previous typhoid infection; none of the autopsied cases have shown typhoid lesions.

Epidemic jaundice, and jaundice with fever, are probably closely related to Weil's disease, which may be described merely as a more intense acute condition. Some observers consider simple jaundice the result of an infection. Enlarged liver and spleen, albuminuria and fever, though slight, can usually be found in these cases.

Acute yellow atrophy with its prodromal symptoms, lack of fever, longer duration, reduction of liver volume, and fatal ending, seems a different condition. Weil's disease may, however, be related thereto. The pathological changes of the latter disease show much more distinctive conditions. Prognosis is favorable when once the diagnosis has been clearly established.

Treatment is purely symptomatic and needs no discussion. *Norman B. Gwyn.*

WEST BADEN SPRINGS.—Orange County, Indiana.

Post-Office.—West Baden Hotel.

Access.—Viâ Ohio and Mississippi Railroad to Shoals, thence by stage or viâ Louisville, New Albany, and Chicago Railroad to Orleans, fifty-six miles north of New Albany, thence by stage to springs. These springs are located in a fine agricultural section, only one mile from the French Lick Springs. The following analysis was made by E. T. Cox, analyst:

One United States gallon of Spring No. 5 contains (solids): Sodium carbonate, gr. 9.69; magnesium carbonate, gr. 6.05; calcium carbonate, gr. 18.62; iron carbonate and aluminum carbonate, gr. 3; sodium sulphate, gr. 31.87; magnesium sulphate, gr. 27.80; calcium sulphate, gr. 108.39; sodium chloride, gr. 81.12; potassium chloride, gr. 6.13; magnesium chloride, gr. 9.20. Total, 301.87 grains. Gases: Carbonic acid, 9.26 cub. in.; sulphureted hydrogen, 2.08 cub. in.; oxygen, 5.28 cub. in.; nitrogen, 15.97 cub. in. The water is used commercially. *James K. Crook.*

WESTPHAL'S SYMPTOM. See *Knee-Jerk.*

WEST SPRINGS.—Union County, South Carolina.

Post-Office.—West Springs. Hotel and cottages.

Access.—From Spartanburg viâ Glenn Springs Railroad, twelve miles southeast to Glenn Springs, thence four miles southeast to West Springs. West Springs are located about 2,000 feet above the sea-level, and are surrounded by picturesque hills covered by extensive forests of spruce, pine, cottonwood, beech, oak, and other trees. The soil is very fertile and many varieties of fruits and vegetables grow in great profusion. Several gold mines are in operation among the near-by hills. There are several springs in the neighborhood, but only one is in use. It yields about four hundred gallons of water per hour. The temperature of this water is 62° F. According to an analysis made in 1893 by M. B. Hardin, analytical chemist, one United States gallon of the water contains (solids): Calcium sulphate, gr. 16.26; potassium sulphate, gr. 1.33; sodium sulphate, gr. 2.75; calcium carbonate, gr. 6.35; magnesium carbonate, gr. 1.17; sodium chloride, gr. 0.21; iron sesquioxide and alumina, gr. 0.03; silica, gr. 2.78; organic matter, a trace. Total, 30.88 grains.

The water is used considerably by South Carolina physicians in diarrhœa and dyspeptic troubles. It is said to possess excellent virtues in chronic catarrhal conditions of the genito-urinary tract—*i.e.*, in gonorrhœa, gleet, leucorrhœa, etc. *James K. Crook.*

WETEMIS MINERAL SPRINGS.—Klickitat County, Washington.

Post-Office.—Blockhouse.

Access.—From The Dalles, Oregon, thirty-five miles by wagon road; also from Goldendale, Washington, eighteen miles distant, by private conveyance.

These springs are new to the public, and no hotel or other accommodations for visitors have yet been provided. Those who visit them during the season, from May 1st to October 15th, are content to enjoy the pleasures of camp life, as excellent grounds for this purpose are at hand. The elevation of the location is 500 or 600 feet above the sea-level, but only a few feet above the Klickitat River, which at this point flows through a grand and picturesque canyon, a thousand feet below the level of the surrounding country. From the brink of the canyon on either side stretches a rolling plateau covered with magnificent forests of pine and fir. A few miles to the southwest lies the wheat-growing region of the Klickitat River, while less than thirty miles north Mount Adams, the second highest peak of the Cascade Range, raises its lofty summit to an elevation of 12,424 feet. The canyon of the Klickitat shelters the springs from the cold winds, while during the summer months clear, warm weather prevails, with occasional rains. The temperature seldom falls lower than —10° or —12° F., while during some winters it does not even reach the zero point. There are three large springs here and several smaller ones, but the water has never yet been analyzed. We are informed that most persons suffering from rheumatism and diseases of the stomach, who have visited the springs, have been much benefited by the water, and some of them apparently cured. Cases of phthisis do well in the neighborhood. Fine hunting and fishing may be enjoyed in the vicinity. It is probable that the spring will soon be developed.

James K. Crook.

WET-NURSES.—At the present day the wet-nurse is by no means the absolute necessity she was in many cases before artificial feeding had reached its present stage of scientific development, so that Holt says that "when one begins with healthy digestive organs, artificial feeding is very simple and almost invariably successful." He refers to the difficulty of securing a suitable wet-nurse and the expense, from $20 to $35 a month in New York, while conceding that she may be essential in certain emergencies, such as acute inanition or acute gastro-enteric intoxication, and that she should be employed in foundling asylums whenever possible. A practitioner may therefore at any time have to decide whether he shall recommend a wet-nurse for a certain infant, and if he decides that question affirmatively he will probably have to determine how to get one, and then to pass on her qualifications for that duty. The physician who wishes to decide this question correctly must approach it from the proper point of view and study it, as he should his obstetrics, from the direction of anatomy and physiology. He will then be firmly impressed with the sound doctrine that, as a rule, maternal nursing is best for the mother and the child. Nor should he forget this fundamental principle, although his decision in the individual case will necessarily be influenced by the many modifying conditions which have always to be allowed weight in settling medical questions. Among these are the feelings, circumstances, and expectations of the family. Other points to be weighed in settling such a question are the residence of the parents, especially in the summer months, the time of year when the child may be ex-

pected to be undergoing dentition, its apparent vigor, and its freedom from hereditary tendency to disease; also any special peculiarities of development manifested by former children of the same parents, if known. Fortunately the structure and traditions of society in this country have not yet become so artificial that we need discuss the custom which prevails in French cities of handing over a baby to a wet-nurse in a remote country district, a practice the demoralizing results of which are traceable in the degeneration of those rural populations most noted for supplying these substitute mothers.

In considering this general subject of wet-nursing the physician may well devote some attention to those causes which, with ordinarily healthy women, especially in the upper walks of society, lead to the inability of such to nurse their babies. In general terms it may, in our own country, be attributed to the increasing artificiality of the life our women lead, and doubtless in part to the great wear and tear of existence in the climate of the United States. In saying this we do not overlook the fact that a more healthful and rational mode of life for the young has been coming into vogue of late. There is, doubtless, a great improvement in the matters of exercise, dress, and food over those which were usual in this country forty or fifty years ago; but the results of such changes must be slow in their development. The great stress and strain are the result of the multitudinous anxieties, cares, and ambitions which are constantly wearing upon the woman of to-day, and of the struggle for improved social position and for wealth, which bore much less heavily upon our grandmothers. Another cause, which it is not easy to estimate correctly, but which is undoubtedly influential, is the want of homogeneity in our people, and the fact that, owing to our migratory national habits, so many are constantly changing their abodes in a country possessed of such a variety of climates, that the race, blended as it is of many nationalities, has in comparatively few parts become identified with its environment. What physician but has been cognizant of many cases in which menstruation has been interrupted in healthy young women for months after immigration? If a change of climate and an unsettling of the mode of life can effect such an alteration in one phase of the generative function, why should they not be powerful in interfering with another phase of it, viz., in causing a diminished activity of the mammary glands?

Having given due weight to the considerations suggested, the medical man, before looking up a wet-nurse for his patient, may well fortify himself by a few thoughts on the objections to wet-nursing, and the very serious dangers it involves. I propose in this place to do no more than call attention briefly to the more prominent of them, trusting that they will be sufficiently brought out incidentally in treating of the different branches of the subject. There is, then, primarily the moral hazard to both mothers, for neither can fully escape the consciousness that her child is deprived of its natural right. Then note the loss to the employing mother of the stimulus of nursing in securing full and healthy involution of the uterus, and consequent freedom from disease of the pelvic organs; also the degree of immunity furnished by maternal nursing against undue frequency of conception and childbearing. On the side of the nurse it is to be remembered that her milk may prove unhealthy for her foster-child, even though it may respond satisfactorily to all the artificial tests we can apply; that grief or fierce passions may make it for the time dangerous to the nursling. Even with the greatest care in choosing them, it is almost impossible to avoid the selection of nurses who are the subjects of syphilis or tuberculous disease. And, finally, the physician and the mother can never be too watchful against the baleful effects springing from the secret use of alcoholic stimulants and of opiates.

Among the risks attending the procuring of a wet-nurse are those due to the irresponsible and mercenary character of the agencies from which they are often obtained. I think it may safely be said that the most desirable women are not to be found in these places; but that, in New York City, one of the two following plans is preferable for securing one: An advertisement in one of the daily papers will commonly bring to the door a superabundance of applicants, of whom a few selected by the family may be asked for references and handed over for medical examination. Or, secondly, inquiry may be made at one or more of the public hospitals or special charitable institutions that maintain a lying-in service, with the great incidental advantage that some accurate account of the nurse's medical history, at least during the puerperal period, can usually be had from the medical officers.

It is undeniable that under some circumstances the employment of a wet-nurse is to be recommended, and it is equally true that this advice is often given under the influence of considerations quite other than simply what would be most beneficial to the mother, the infant, or even the proposed nurse. The doctor should realize that, in order to nurse her baby, a mother must restrict herself in many ways, must be regular in her hours, which involves the loss of many pleasures which women covet, must in fact sacrifice herself for her child. Nursing, when undertaken, is a duty, the demands of which are imperative and cannot be postponed with safety to either party concerned. Diet, exercise, clothing, mental and moral habits should all be subordinated to the proper discharge of this function, though fashion and social ambition are leagued in strong opposition. This is the view that the physician should uphold and encourage. He can do more than any one else in the community to foster in the mind of every woman whom he attends during pregnancy or confinement the idea that lactation is the necessary and proper complement and rounding-out for her of the great physiological cycle which begins with conception; and the woman who follows this advice and makes these sacrifices will not need a physician to point out to her the benefits which accrue to herself and her offspring, physically, mentally, and morally, from the course adopted.

The conditions which preclude maternal nursing are briefly summed up by Lusk, as follows: "Nursing may be rendered impossible by a lack of milk, by flattened, misshapen nipples, and by the health of the mother. It should be prohibited in phthisis, in epilepsy, and in cases of syphilis contracted shortly before the birth of the child."[1] Bumm says that from fifteen to twenty per cent. of mothers cannot nurse their children.

It is well for the physician to appreciate the influence exerted by the monthly nurse, who should in this matter be his ally, and not, as is too often the case, the wily and underhanded opponent of his best efforts to make his patient nurse her babe. So potent is this influence that certain of these women come to be known as always having their charges nurse their infants, and others as always finding that they cannot do so, a reputation which may well guide the physician in passing on their qualifications.

If such care of herself as I have indicated is to be expected in the case of a mother nursing her own child, let us now apply the rule inversely and see what we should look for in a woman who is proposed as nurse to another's child, and what rules should be laid down for her guidance when acting as wet-nurse.

One of the first questions to be decided is whether we should refuse our recommendation to an unmarried woman, who may prove in all other respects well qualified. A great deal can be said on both sides of this question, but as it hinges largely upon the moral point involved, my own view is that, in so far, it is one the decision of which should not be thrown upon the medical man. The mother, or female head of the family in which the wet-nurse is to serve, would never consent to surrender her convictions on such a point, nor would a prudent physician care to assume the responsibility of introducing such a woman in opposition to the ideas of the family. Still he may be asked for an opinion as to how far, or in what ways, the fact of the applicant being single would influence her desirability as a wet-nurse, and he

should be ready to state them. We cannot be guided by foreign opinion, for we all recognize the fact that pregnancy in the unmarried is not regarded with the same leniency here as in many parts of Europe, and that consequently the status and morale of such as have incurred it are relatively lowered. We therefore feel that such a woman, while an object of pity and deserving of all charitable consideration, is not unadvisedly to be brought into a family in a position which is regarded as superior to that of other servants, where she will come into close relations with the children and the mother, and where weakness of character and lower tone might have the most serious results. On the other hand, where the family is disposed to overlook these drawbacks, especially where there are no older children, or to regard the interests of the nursling as paramount to, or as dominating all other considerations, it may be looked upon as a favorable feature that the unmarried wet-nurse is not subject to the claims of a husband or a family, which are often advanced at most inconvenient seasons, and with the palpable design of profiting by the necessities of the employer; also that, except in the case of the very depraved, lactation is less likely than in the married to be interrupted by a recurrence of pregnancy. In the unmarried there would, besides, usually be such advantages as accrue from the engagement of a primipara.

The age of a wet-nurse is not immaterial, and, while not unmindful of recorded facts, or those known to individual experience, where young girls or women advanced in life have proved excellent nurses, it still remains a safe rule to avoid the extremes of the child-bearing period and to give the preference to those between twenty and thirty, or, possibly, thirty-five years. This would be, of course, with the view of avoiding immaturity and constitutional vices of tardy development on the one hand, and, on the other, the disabilities connected with physical exhaustion or possible degeneration.

The age of the milk should bear some relation to the age of the child to be nursed, for, though a deficiency of the laxative qualities of the colostrum may be made good by suitable medicines, there is always danger, if the milk is much older than the child, that the supply may not last as long as desired. On the other hand, the quality of the secretion is, after the first few weeks, comparatively uniform for months, so that it will be little likely to disagree on that account even when the child is older.

As between a primipara and pluripara, other things being equal, the choice would be in favor of the latter, for the reason that her previous experience should have taught her something about the proper care of an infant, and some estimate might likewise be made of the probable continuance of the milk supply in her case.

We now come to the physical examination of the proposed wet-nurse. The physician should make this as thorough as he has opportunity for, although he will seldom in private practice be able to complete it by examining the genitals. Still, if the woman has been confined in a hospital, valuable information on this point may be obtained from the house physician. A general survey of the applicant's physique, expression, cleanliness, etc., should be followed by special observation of the temperature, eyes, teeth, tongue, breath, fauces, skin —especially on the neck and breasts; also of the lungs and heart and the lymphatic glands of the neck and at the bend of the elbow. One should try to ascertain whether pregnancy does or does not exist, and the inquiry should be made whether menstruation has taken place, albeit the latter question may often not elicit a truthful answer and the fact will have to be learned by subsequent careful observation. It is especially important to ascertain the presence or absence of indications of any form of tuberculosis, of anæmia, or of syphilis. Rheumatism also must not be forgotten. The breasts should receive special attention; they should be full and hard three hours after nursing (Holt). The size and firmness of the mammary glands themselves should be distinguished from accompanying adipose deposits; the skin should show the course of the large veins running from the areolæ, and it should be free from cicatrices or discolorations pointing to former abscesses or eruptions; the nipples should be of good size and prominence, without evidence of irritability or of loss of substance from former ulceration. Pressure should cause the milk to flow readily in numerous jets. A specimen of it should be obtained for chemical and microscopical examination, and, finally, the woman's own child, if nursed by herself alone, should be seen and carefully examined. Nothing can be better evidence of the value of the mother as a nurse than the condition of her own child; but it behooves the physician to be on the watch for substitution and other deceitful practices. Should it be possible, let him watch the child nurse. Then he can learn whether the milk flows easily and in abundance with but moderate effort on its part, and whether the child lets go of the nipple with an air of comfort, its lips dripping with the over-abundance of milk, or whether it repeatedly rejects the nipple unsatisfied and disappointed.

The milk itself should, of course, be examined as to both its physical and its chemical qualities. As to the former, Eustace Smith writes as follows: "The milk should be opaque and of a dull white color; under the microscope it should present fat globules of medium size, not too small. As a rule, the number of fat globules is a rough indication of the quantity of casein and sugar, though not always a trustworthy guide."[2] A more systematic and thorough method is quoted by Jacobi from F. Conrad (Bonn, 1880). He draws the milk himself two or three hours after the last nursing, making use either of the breast-pump or of pressure by the thumb and index finger. This latter manipulation, after a little practice, causes no pain and makes it possible to appreciate the abundance and easy discharge of the secretion. He then determines: (1) The reaction, which should always be alkaline. (2) The specific gravity, which should be from 1.025 to 1.035; with an average of 1.031. (3) The microscopical appearance. The milk globules should be well formed, separate from each other, from 0.0088 mm. to 0.198 mm. in size, and those of medium size should predominate.[3]

Bumm quotes J. Koenig's recent analyses as showing the following chemical constitution: Sugar of milk, 6.21; milk fat, 3.78; albumin and casein, 2.29; salts, 0.71.

A wet-nurse having been chosen and her milk found to agree with her foster-child, the interests of all require that her mode of life should be so ordered as to keep her in the best condition for discharging this function. The error most likely to be committed is in changing too much her diet and régime, partly because the employers do not realize how the way of life and the kind of food to which she has been accustomed differ from their own, and partly because the nurse, finding food and other comforts in kind and quantity far exceeding those of her own home, and having withal a hearty appetite and the plausible excuse that the baby depends upon her, overindulges herself. The not uncommon result is that she grows enormously fat and at the same time loses the power to furnish the abundant supply of good milk which constituted her value. Rotch tells us that by improper feeding the quality of the milk may be changed so as to resemble cow's more than human milk in the amount of solids. This state of things leads to an attempt, probably surreptitious, to force a greater secretion by drinking beer or other alcoholics, and the downward course is begun which is not unlikely to end in the discharge of the nurse, either immediately before or after the death of the baby in convulsions. A rational management should forestall such catastrophes. In the first place, then, make the nurse bathe thoroughly and sufficiently. See that she has enough, but not too much, food of a nutritious kind and largely liquid, with an amount of exercise proportioned to her previous habits of life. Do all that is possible to secure her peace of mind and good spirits, especially by attending to the welfare of her own child, if it is living. Without going into particulars as to diet, we may say that it should be so ordered by the medical adviser as to be fully capable

of replacing in the system the materials required by the secretion of milk, viz., fats and the various forms of albumin. Salts or salines should not be used largely as food or medicine, nor should articles containing strong-smelling oils. Milk is particularly good as food, while alcoholics should be avoided, unless, perhaps, a small quantity of beer for women who have always been accustomed to it in their own country.

Further details on wet-nursing may be found in the treatises on obstetrics and pediatrics. Among the works mentioned below I would call particular attention to those of Rotch and Holt. *J. Haven Emerson.*

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WHANN ALKALINE LITHIA SPRINGS.—Venango County, Pennsylvania.

These springs issue from the rocky bluffs 200 feet above the Allegheny River, at a spot which commands a fine view of the charming little city of Franklin. Their high altitude and spacious woodland surroundings preclude the dangers of surface contamination. The outflow is abundant and the water clear, bright, and sparkling. Its temperature at the springs is 50° F. all the year round. The following analysis was made by Merck & Co., chemists, of New York, in 1899:

One United States gallon contains (solids): Lithium chloride, gr. 3.68; sodium chloride, gr. 3.77; calcium carbonate, gr. 3.09; magnesium carbonate, gr. 0.75; magnesium sulphate, gr. 1.17; sodium sulphate, gr. 0.16; potassium sulphate, gr. 0.30; aluminum sulphate, gr. 0.07; silica, gr. 0.69. Total solids, 13.68 grains. Total residue by evaporation, gr. 15.09; organic matter and loss on ignition, gr. 3.68; carbon dioxide, free, gr. 1.37; nitrites and nitrates, traces.

The analysis shows a light alkaline-saline water which on habitual use ought to possess useful properties as an antacid, diuretic, and possibly laxative. It has been highly praised by physicians, who have become acquainted with its use, in rheumatism, gout, dyspepsia, and gastro-intestinal disorders, and in the uric-acid diathesis. *James K. Crook.*

WHEAL. See *Urticaria.*

WHIP-WORM. See *Nematoda.*

WHITE SULPHUR SPRINGS.—Scott County, Iowa.

Post-Office.—White Sulphur. Hotel destroyed by fire in 1893.

The waters of these springs are now used commercially. The following analysis was made by Emory Rush, of Buffalo, N. Y. One United States gallon contains (solids): Sodium chloride, gr. 92.79; calcium chloride, gr. 33.56; magnesium chloride, gr. 23.26; sodium bicarbonate, gr. 40.57; iron bicarbonate, gr. 27.37; potassium sulphate, gr. 6.13; sodium phosphate, gr. 5; silica, gr. 30.56; magnesium sulphate, gr. 16.23; carbonic acid (by weight), gr. 31.57. Total solids upon evaporation, 307.04 grains. Temperature, 56° F.

James K. Crook.

WHITE SULPHUR SPRINGS, LOUISIANA.—Catahoula Parish, Louisiana

Post-Office.—White Sulphur Springs. Hotel.

Access.—The springs are reached by way of Alexandria, La., on the St. Louis, Iron Mountain and Southern, and the Southern Pacific Railroad, or by way of Pollock Station, on the Iron Mountain Railroad. The location is in a hilly country, covered with pines. The springs are four in number, and, according to Mr. G. W. Bethards, of the Railroad Hotel, their combined flow is about thirty thousand gallons per minute. Like many other enterprises in the South, the resort lacks capital for its improvement. No analysis has been made, but the water has been used with apparent benefit in rheumatism, dyspepsia, Bright's disease, and debility.

James K. Crook.

WHITE SULPHUR SPRINGS, MONTANA.—Meagher County, Montana.

Post-Office.—White Sulphur Springs. Hotel.

Access.—By Northern Pacific Railroad to Townsend, thence by stage or private conveyance to the springs. They may also be reached by stage from Helena, seventy-five miles distant.

The springs are located at an elevation of 5,012 feet above the sea-level, in a valley seventy-five miles long by ten or fifteen wide, watered by numerous streams where trout and other fish are abundant. Game is also plentiful in the surrounding mountains. An analysis by R. B. Riggs, of the United States Geological Survey, in 1885, showed the presence of the carbonates of sodium, calcium, and magnesium, sulphate of sodium, chlorides of sodium and potassium, silica, and a trace of sulphureted hydrogen. The water is of the alkaline-saline-thermal type. The temperature of the water varies from 95° F. to 125° F. It is recommended for affections of the liver, for skin diseases, and for syphilis.

James K. Crook.

WHITLOW. See *Hands and Fingers, etc.*

WHOOPING-COUGH is a specific infectious disease characterized by paroxysmal attacks of coughing followed by deep inspiratory efforts, which, owing to a spasmodic contraction of the glottis, have a loud crowing or whooping sound.

Synonyms.—Whooping-cough, hooping-cough, pertussis, Keuchhusten (Ger.), coqueluche (Fr.), pertosse (Ital.), Kikhosta (Swed.), chincough, kindcough, kinkcough, kinkkaust, Kinghost, Stickhusten, Krampfhusten, Blauer-husten, Hühnerweh, Eselhusten, Rehhusten; toux convulsive ou quinteuse ou bleue, maladie cucullaire, paroxysmes quintes, architoux des enfants; tussis ferina, seu convulsiva, seu strangulans, seu quinta, seu stomachalis; anhela clamosa, seu strangulans, seu delassans, seu suffocans, seu amphemerina, seu tussiculosa, seu spasmodica, seu asinina, seu canina, seu perennis, seu clangosa, seu puerilis; tussis epidemica puerorum; bronchitis convulsiva, bronchocephalitis, pneusis pertussis; orthopnœa tussiculosa, seu clangosa, etc.; morbus cucullus, seu cucullaris; cucullus; bex convulsiva, seu theriodes; bechorthopnœa.

History.—It is generally admitted that whooping-cough was unknown to the ancients, as no description of the disease is to be found in the writings of Hippocrates, Galen, or Avicenna.

The first account we have of the disease is by Baillou or Ballonius, a Frenchman, in 1578. He called it *quintes* or *quintana*, as the paroxysms of coughing were supposed to occur at intervals of five hours. Schenck, of Grafenberg, described the disease some years later. In England there was no definite account of whooping-cough till 1667, when Willis gave a very clear description of it under the name of *tussis puerorum convulsiva;* he was followed later by the famous Sydenham. Ettmüller, in Germany, and Lieutaud, in France, also published short accounts of the disease in the seventeenth century, at which time it occurred apparently only in small epidemics, although Willis speaks of its frequent occurrence among children and of the considerable mortality caused by it.

The first entry in the London mortality returns of a

death from this disease, under the name of chincough, is in the year 1668.

Throughout the eighteenth century whooping-cough rapidly increased and became widely diffused, as numerous descriptions of epidemics attest. In Sweden, from the year 1749 to the year 1764, over 43,000 children were said to have succumbed to this disease. In England, Germany, the Netherlands, Switzerland, Italy, and America, numerous epidemics prevailed.

At the present time whooping-cough not only occurs epidemically throughout Europe and America, but in nearly all the large cities and towns it has become endemic, so that cases are almost continuously occurring. In England, out of a total mortality of 510,315 in 1876, 10,556, or nearly two per cent., were due to this disease. In 1880 the proportion of deaths from whooping-cough in England was 2.59 per cent. Biermer says "whooping-cough has become a disease of all races and climates."

Symptomatology.—Whooping-cough has been divided into three stages, which are more or less distinctive in various cases, and which pass more or less gradually from one to the other. These are, first, the catarrhal or prodromal stage; second, the paroxysmal or spasmodic stage; third, the stage of decline.

The catarrhal stage begins as a catarrh of the upper respiratory tract, and resembles an ordinary cold, from which, indeed, it cannot as a rule be distinguished, and it is often necessary to wait for the second stage before a definite diagnosis can be made. The prevalence of whooping-cough in the neighborhood or the history of exposure puts the physician on his guard. The symptoms in this stage are an ordinary cough, usually rather severe, and with a tendency to become paroxysmal, more or less coryza, with sneezing, and sometimes slight watering of the eyes, due to a mild conjunctivitis. An elevation of temperature occurs in this stage, which, although slight, is generally greater than in ordinary bronchitis, and is regarded by Flint, therefore, as an idiopathic or essential fever, as distinguished from a symptomatic one. Henoch, however, considers this idea of an essential fever to be erroneous.

The duration of the first stage is generally ten days or two weeks, but it varies markedly. The younger the child, the shorter is the first stage. Besides the factor of age, the severity of the attack also influences the duration of the prodromal stage. Thus the more severe the attack the shorter the first stage is likely to be; and, on the other hand, in mild cases the first stage may be lengthened to three or four weeks, or even in some cases may terminate without passing into the second stage, the diagnosis in these exceptionally mild cases being made by the existence at the same time of well-marked cases in other members of the same household.

The second stage, into which the first gradually or at times abruptly glides, is characterized by paroxysms of rapidly repeated forcible expiratory efforts or coughs, followed by a deep inspiration, which, owing to the spasmodic contraction of the muscles of the larynx causing a narrowing of the rima glottidis, has a loud and peculiar crowing or whooping sound, from which the name of the disease is derived. The little patient is generally conscious of an impending attack, becomes restless, and awakes from sleep, or, if at play, drops its toys with an expression of apprehension, and often appears to make every effort to suppress the approaching paroxysm. The pulse and respirations become more rapid, and when the coughing begins the child seeks to grasp its mother or some firm object for support. The respiratory efforts, from five to twenty in number, follow each other in rapid succession, terminating in a deep-drawn inspiration or whoop, and, after a rapid repetition of the series two or three times, there generally occurs the expulsion of a thick, glairy, tenacious mucus, and often the vomiting of the contents of the stomach, after which the child sinks back exhausted, but, if in a good condition, soon resumes its play as if nothing had happened. The urine and fæces are not infrequently expelled involuntarily in young children, owing to the violent action of the diaphragm and abdominal muscles. Older children, who are able to describe their sensations, and adults speak of a feeling of heaviness or oppression in the chest, and of an increasing tickling sensation in the throat, or the sensation of a foreign body in that region, which lead them to expect a paroxysm. A tickling in the nose or, in some cases, the feeling of nausea is also sometimes described by the sufferers as presaging an attack. The spasm of the glottis, and therefore inspiratory whoop, is more marked when the expiratory efforts have been violent and have followed each other in rapid succession.

During the expiratory efforts the pulmonary circulation is impeded, and a backing up of blood in the right side of the heart occurs, with resulting venous stasis. The veins of the neck become distended, the face reddened, and, finally, from the interference with respiration, cyanotic. The eyes stand out and are suffused with tears, the loose connective tissue about the eyes is puffy with infiltrated serum, and in severe paroxysms hemorrhages may take place from the nose or mouth, or subconjunctival ecchymoses may appear. The tongue in infants and young children is generally violently protruded from the mouth, the frænum and lower surface scraping against the gums or teeth. The child often makes clutches at its throat and face, and endeavors to relieve itself by pulling the mucus from its mouth. In these attempts the infant, with its poorly co-ordinated movements, will sometimes scratch its neck and face, or the mucous membrane of the mouth.

After the paroxysm the cyanosis is succeeded by pallor, the distended blood-vessels empty themselves, but the puffiness about the eyes, due to the infiltrated serum, often remains as a characteristic feature. Sometimes the child is covered with a cold sweat after the paroxysm.

The duration and severity of the paroxysms may be so slight that many of these symptoms are lacking, and the expiratory efforts may be only one or two in number. On the other hand, the attack may last one or even two minutes, consisting of a number of series of expiratory efforts, causing marked cyanosis and distress, and leaving the patient in a very exhausted condition. The number of paroxysms in twenty-four hours also varies very much, from two or three in very mild cases to fifty or even a hundred in the more severe examples. A characteristic feature of whooping-cough, and one that is almost always present, is the fact that the paroxysms are more common at night than during the daytime. In the waking hours any emotional excitement is apt to bring on the cough; hence this is frequently observed during the visit of the physician. A fit of crying is almost sure to be interrupted by a paroxysm of cough, which, by substituting a greater evil, effectually removes the original cause of the tears from the mind of the little patient. In a similar way, with several children in a room all suffering from this disease, the occurrence of a paroxysm in one is apt to be followed by the same thing in the others—the so-called paroxysm from imitation.

The fever, which may have been present in the first stage, is now generally absent, although an occasional temperature of 101° or 102° F. in the evening is not at all uncommon. A continuously elevated temperature, on the other hand, would at once point to some complication.

Vomiting following the paroxysm may be so frequent as seriously to interfere with the nutrition of the patient. In these cases the stomach becomes so sensitive that a very slight cough may be followed by the evacuation of the entire contents of the stomach; whereas in earlier periods of the same case or in milder cases vomiting occurs only after violent paroxysms. The general condition of the patient during the intervals between the attacks, supposing there are no complications, remains good if the course of the disease is mild; but if severe, the patient becomes much emaciated and debilitated.

The duration of the second stage varies very much, but averages from four to eight weeks, and gradually merges into the third stage, or stage of decline, when the cough has become less frequent and has ceased to

be spasmodic. This stage lasts generally two or three weeks, but is apt to be interrupted and prolonged by returns of the old paroxysmal cough. In fact, for a year or two after an attack of whooping-cough, an ordinary bronchitis is apt to take on the spasmodic character of the former disease.

When uninfluenced by treatment, therefore, whooping-cough runs a course of from two to three months. A duration of less than six weeks is uncommon, while one of more than three months is unfortunately less so. An average of ten weeks, as stated by West, is probably as accurate an estimate as can be given.

The physical examination in an interval between paroxysms of cough will show, in uncomplicated cases, more or less emaciation and anæmia dependent on the severity of the attack, possibly slight puffiness of the face, especially about the eyes, and in some cases an excoriation or ulcer on the frænum linguæ, with perhaps a slight bronchitis. In mild cases of whooping-cough there may be an entire absence of these signs, and the child may appear to be in perfect health during the intervals of the cough.

Sugar is occasionally found in the urine. Dolan found traces in fourteen out of fifty cases examined on this point. Albumin may also occasionally be found.

Complications.—The principal complications of whooping-cough may be divided into three classes: first, those due to an increase or extension of the mild inflammation of the air passages, which probably accompanies all cases of whooping-cough; secondly, complications due directly or indirectly to the paroxysm of coughing; and thirdly, accidental complications.

Bronchitis, although generally present in whooping-cough, is always, even in its mildest form, considered a complication by some authors. This bronchitis may increase and involve the smaller capillary tubes, especially in debilitated children and where the hygienic surroundings are poor, and result in bronchopneumonia. This is the most serious complication and is largely responsible for the mortality. With the presence of bronchopneumonia the little patient can ill bear the paroxysms of cough, but these fortunately, as a rule, become less severe at this time, so that false hopes are thereby excited.

Of the complications due to the violent paroxysms of cough may be mentioned pulmonary vesicular emphysema. Its diagnosis during life is often impossible, but the condition is frequently seen at post-mortem examinations, especially in the upper lobes of the lungs.

A more extreme condition rarely occurs, namely, rupture of the air cells, giving rise to interlobular emphysema. In these cases the air is sometimes forced into the loose connective tissue of the neck or even of the entire body.

According to Strümpell, a lobular emphysema may sometimes persist as a chronic state after recovery from whooping-cough.

Another group of complications that may result from violent paroxysms of coughing are hemorrhages. Epistaxis is the most frequent form, and may in some cases be so severe as greatly to enfeeble the patient or even to prove fatal. The next most common source of hemorrhage is the mouth, either from the ulcer or abrasion under the tongue, produced by friction against the lower incisors, or from the dry and cracked lips which are rubbed or picked by the little patient, or from the gums, tongue, pharynx, or indeed from any part of the buccal cavity. If stomatitis exist, the facility for bleeding is of course increased. In cases of bleeding from the mouth, the mucus, which is churned about in the mouth before it is expelled, becomes of course blood-stained, or the patient even spits out pure blood, if the hemorrhage is sufficiently free. This alarms the parents much more than a copious epistaxis would do, and they send for the doctor at once, thinking the child is coughing up blood from the lungs. True hæmoptysis, however, is very rare in children under ten years of age, and even in tuberculous cases is seldom seen at such an early age.

Subconjunctival hemorrhages are not uncommon and give no pain, neither do they interfere with vision. They are almost diagnostic of this disease, as they are rarely seen in children from other causes, trauma of course being excluded. A conjunctival hemorrhage is rare. Trousseau reports a case in which it gave the appearance of tears of blood. Vision may be partially or totally obscured by hemorrhage into the retina. Blindness in whooping-cough has been found in some cases to be due to ischæmia retinæ. Exophthalmus from hemorrhage behind the ball has been observed, also subluxation of the lens due to partial rupture of the zonula Zinnii in a fit of coughing.

Otorrhagia is very rare, and is due to the rupture of the membrana tympani by the air being violently forced up the Eustachian tube during coughing, or by the rupture of the vessels of the external auditory canal, which have been altered by an acute or chronic inflammation.

Subcutaneous hemorrhages, or ecchymoses, occasionally occur.

Hemorrhages of the brain or meninges, as is natural to infer, occur from the same causes as hemorrhages elsewhere, although they are rare and are of very serious and often fatal import. The history is usually that of a severe paroxysm of cough, followed by paralysis and loss of sensation in various parts, often a hemiplegia with unconsciousness and convulsive movements. The symptoms may gradually increase in severity, pointing to a slowly progressing hemorrhage. Very serious and ominous symptoms may be followed by complete recovery, so that the physician must not hurriedly give a fatal prognosis.

Convulsions in whooping-cough are, however, often due simply to the general reflex disturbance, owing to the high state of tension of the nervous system in children; but cerebral or spinal congestion, resulting solely from the cough, may be, and frequently is, a cause of the convulsions.

Hernia of the bowels and prolapsus ani are not infrequently seen, resulting from the strong expiratory efforts; and, rarely, the rupture of the rectus abdominis with the formation of a large tumor.

Etiology.—The infectious nature of this disease demands a living organism as the causative agent, and observers all over the world have been busy on this problem.

Deichler, in 1886, found always present in the sputa of whooping-cough patients an amœba-like protozoon. This has been confirmed more lately by Kinloff, and again by Behla, but the importance of this organism in the etiology of the disease may perhaps be doubted.

Afanassieff, in 1887, found in the sputa short, rod-like bacteria of 0.6 to 2.2 μ in size, from which he obtained pure cultures, and states that this bacillus—"Bacillus tussis convulsivæ"—is distinctive from any previously described bacterium. With the pure culture he made eighteen experiments on animals by injecting it into the trachea or lungs, by which he produced in all cases symptoms of whooping-cough. On post-mortem examination of these cases he states that these bacteria were found on the mucous membrane of the bronchi, trachea, and nose, and he also found the same germ on the mucous membrane of the respiratory passages of children who died of whooping-cough.

Since then Ritter, Zusch, Czaplewski and Hensel, and Koplik, have all isolated and studied a bacillus which is perhaps identical with that first described by Afanassieff.

Czaplewski and Hensel worked out a method which did not fail to show this characteristic bacillus in every case. They described the bacillus as being oval with rounded ends, which sometimes stain more deeply than the centre, giving the appearance of a diplococcus.

Whooping-cough is contagious during its whole course, especially during the first or catarrhal stage. It is least contagious during the third stage, or stage of decline, and its contagiousness may cease while the cough, which is then due to a simple bronchitis, still continues. The contagiousness may even cease before the whooping has stopped, for this latter may be kept up simply as a nervous habit. So-called relapses, where the spasmodic

attacks return during mild bronchial catarrhs acquired shortly after the whooping-cough has ceased, are generally to be explained in the same way, and are therefore not contagious. One attack of the disease secures immunity from it for the future, yet two or more distinct attacks of the disease in the same individual may sometimes, though rarely, occur.

Whooping-cough is very rarely carried by a third person or by the medium of clothing. Roger gives an instance of a boy sick for a long time with typhoid fever, never in contact with a case of whooping-cough, and yet developing that disease. The father and the doctor were the only ones who saw the patient, and therefore one of these must have acted as the medium for conveying the poison of the disease. I have recently seen a case in which the evidence of transmission by a third person was very clear. Clothing stained with sputa, it would seem, might easily convey the disease, although facts on this point are lacking. It is probable that the poison does not long survive outside of the body.

Like all contagious diseases whooping-cough prevails at times epidemically, and sporadic cases are to be traced to some previous case. Most large towns and cities are never entirely free from the contagion of this disease and cases exist at all times; or, in other words, whooping-cough is there naturalized or endemic. After a year of unusually great prevalence of whooping-cough in any large town or city, the number of cases in the following year is generally much less, a fact easily explained, as there are comparatively few children who are not protected by having suffered from the disease the year before.

The period of *incubation* varies considerably, but is generally from four to ten days in length.

Whooping-cough may occur in the new-born infant and in the aged, but is most common between the ages of one and five years.

In fact, owing to the almost universal prevalence of whooping-cough, very few children escape the disease, and this fact sufficiently accounts for its infrequency in adult life.

There are a few cases recorded in which the infant was born with the disease, the fœtus being infected in the uterus from the mother who was suffering with the disease.

As to the season of the year, one would expect to find whooping-cough more prevalent in the winter, owing to the greater chances of infection by aggregation of children in schools, and the imperfect ventilation that prevails in this season as compared with the summer. Hirsch, however, has shown that the seasons have no influence on the spread of this disease.

Pathology.—Post-mortem examinations in cases of whooping-cough almost invariably show the morbid anatomy of some complication, as death from the disease alone is almost unknown. In the latter case we would find evidence of slight catarrh of the air passages, so slight and superficial as to be scarcely noticed. Examinations during life by means of the laryngoscope give us the most satisfactory knowledge of the pathological changes, and these studies have been made by observers, partly on themselves while suffering from an attack of whooping-cough, and also on others. The most elaborate and complete observations of Meyer Hüni and von Herff are in the main similar. They found a superficial inflammation or catarrh of the mucous membrane, from the nose and pharynx to the bifurcation of the trachea. The inflammation was found most marked on the posterior wall of the larynx, on the arytenoid cartilages and those of Santorini and Wrisberg, and especially in the interarytenoid region, and also on the under surface of the epiglottis. The vocal cords were intact. The posterior wall of the larynx, as high as the vocal cords, constituted the so-called "cough region"; that is to say, irritation of this part by flecks of mucus, or artificially by a laryngeal probe, as shown by von Herff, always brought on a violent paroxysm of cough. A similar but less intense one was produced by irritating the lower surface of the epiglottis, while touching other parts of the larynx never brought on a true paroxysm. Flecks of mucus were seen by these observers to bring on a paroxysm of coughing, when they reached the opening of the glottis, which continued till they were expelled. During the violent inspirations the incoming air draws down the partially coughed-up bronchial secretion, renewing the irritation, and again bringing on a paroxysm, and the series ceases only on the complete expulsion of the mucus, or until, through exhaustion, the irritability is dulled. Meyer Hüni thinks that there is also probably another "cough region" at the bifurcation of the trachea.

Rossbach's observations, however, differ entirely from these, for he found the pharynx, larynx, and upper two-thirds of the trachea normal, without either redness or swelling of the mucous membrane. A catarrh of the larger bronchi, however, he considered a part of the disease, and just before a paroxysm he saw bubbles of mucus coming up from the lower part of the trachea.

Besides the superficial catarrh, involving more or less of the upper air passages in mild cases of whooping-cough, pathological changes are absent. The ulcer sometimes found under the tongue was at one time thought to be the specific lesion of whooping-cough, but is now recognized to be due to the friction of the tongue against the lower incisors, when it is violently thrust out in a paroxysm of coughing.

Diagnosis.—During the first stage the diagnosis of whooping-cough is impossible in the majority of cases. The history of exposure to the contagion of whooping-cough, in a patient not protected by a previous attack, should make the physician suspicious of this disease when he finds a cough with few or no signs of bronchitis, especially if there be an elevation of temperaure out of proportion to the severity of the bronchitis. During the prevalence of an epidemic, all cases of cough not due to any well-recognized cause, in children unprotected by a previous attack, should always arouse the suspicions of the physician, and the possibility of the disease should be mentioned to the parents, so that they may be on the lookout for the whoop. Whooping is, indeed, the characteristic symptom of the disease, but is not heard till the second stage has been reached, and when this is well marked the diagnosis is easily made. The visit of the physician often excites the child so that a paroxysm is induced, making the diagnosis plain. Pressing on the larynx or the root of the tongue, or on the vagus nerve at the base of the neck, or making the child cry, may be resorted to for diagnostic purposes to bring on a paroxysm of coughing.

In infants under six months of age, and in very mild cases in older children, the diagnostic whoop is often absent. Here we must depend on the history of exposure to contagion, on the history of a quiescent or incubative stage, and on that of a prodromal catarrhal stage; on the paroxysmal character of the cough, generally more frequent at night; on the congestion of the face during the paroxysm, the expectoration of the characteristic glairy, tenacious mucus, and the vomiting of the contents of the stomach. Whooping-cough is, indeed, the only disease in infants in which there occurs actual expectoration of abundant mucus.

The appearance of the child in the intervals between the paroxsyms is almost diagnostic in cases in which the course of the disease is severe. In these cases we find pallor, more or less emaciation, puffiness under the eyes, congestion of the conjunctivæ, and, in a certain proportion of the cases, abrasions or ulcerations of the frænum linguæ. Subconjunctival ecchymoses in children are almost pathognomonic of whooping-cough, as they are rarely seen in them from any other cause excepting traumatism.

In many cases it is a very difficult matter to decide whether a patient has whooping-cough or merely a bronchitis with copious secretion of mucus, causing suffocative or spasmodic attacks of coughing. Here we must carefully consider all the points mentioned above, and treat doubtful cases as cases of the disease until the diag-

nosis is clear, isolating them as much as possible, and refusing to admit them to the open wards of hospitals or other institutions.

Recently Meunier has pointed out a method for early diagnosis, namely, the constant leucocytosis which he has found in this disease, one that far exceeds the leucocytosis found in other febrile affections of the respiratory tract. The leucocytosis begins early, before the appearance of the typical paroxysms, and averages 25,000, reaching later as high as 40,000. Fröhlich found that the leucocytosis kept pace with the number of kinks. Wanstall has not confirmed these statements, he finds, however, an increased percentage of lymphocytes, at least equalling or exceeding that of the polynuclear neutrophilic cells, which he considers of diagnostic importance.

A method for certain early diagnosis of whooping-cough would be of the greatest practical service.

Prognosis.—The prognosis in whooping-cough is very favorable if the general health of the patient is good and there be no complications. The occurrence of the latter, moreover, is largely dependent on the former, for the stronger the patient the less liable is he to complications, and death, in the absence of complications, rarely occurs.

Of the complications which cause death, by far the most common is lobular or broncho-pneumonia. The little patient may also die from exhaustion and malnutrition induced by the protracted course of the disease, the disturbed sleep, exhausting attacks of coughing, and starvation owing to the frequent vomiting. Hemorrhages from mucous membranes add greatly to the debility, and may in themselves prove fatal. Owing to the feeble state induced by these causes, the prognosis in intercurrent diseases is made much more unfavorable.

The prognosis in those already weakened by chronic disease or by previous acute disease is also more unfavorable; especially is this the case if the acute disease has left the bronchial mucous membrane impaired, as in the case of measles, for the patient is then more liable to complicating bronchitis which may eventuate in a severe broncho-pneumonia and death. Broncho-pneumonia is, indeed, the final act in a large proportion of the fatal cases of whooping-cough.

Convulsions are always of unfavorable import, whether they be due to the reflex irritability, to congestion and œdema of the brain, or to cerebral hemorrhage.

The age of the patient influences the prognosis very much; for the older the children the better able are they to withstand the exhausting effects of the disease, and the less liable are they to complications.

In adults the disease runs, as a rule, a moderate course, and the prognosis is good unless other unfavorable conditions exist. In the aged we again return to the feeble state similar to childhood, when resistance to disease is impaired, and here the prognosis may become unfavorable.

In Basle, according to Hagenbach, the mortality by ages, during eleven years, was as follows: Under one year, 26.8 per cent.; one to two years, 13.8 per cent.; two to five years, 3 per cent.; five to ten years, 1.8 per cent.; ten to fifteen years, 1.8 per cent. Biermer estimates that 31 per cent. of the fatal cases of whooping-cough occur in the first year of life.

As to sex, the prognosis is slightly more unfavorable for females than for males.

Dolan states that whooping-cough causes one-fourth of the annual mortality among children under five years in London.

In the United States, according to the census of 1880, the list of deaths from infectious diseases is as follows:

	Under five years.	At all ages.
Deaths from diphtheria	19,854	38,143
Deaths from whooping-cough	10,313	11,064
Deaths from scarlet fever	10,142	16,388
Deaths from measles	5,181	8,062

The United States census of 1880 also shows a greater proportion of deaths in the rural districts (16.9) than in the large cities (9.7), and, in the regions where a distinction of color was made, a much greater proportion among the colored (33), than among the whites (14.3).

The census also shows the largest proportion of deaths to the total mortality to occur in the Appalachian region, comprising portions of Virginia, West Virginia, Kentucky, Tennessee, and Alabama, and on the Southern Atlantic coast, from the mouth of the Chesapeake Bay to the northern boundary of Florida, including both Carolinas and Georgia. The smallest number of deaths occurred in New England, New York, and Pennsylvania, the proportion there being under ten in one thousand deaths from known causes.

According to the United States Census of 1860, 1870, and 1880, comprising 17,939 cases, the greatest mortality from whooping-cough occurred in March, April, and May, and the least in October, November, and December.

Treatment.—As in all diseases which are prevalent, which are obstinate to treatment, and which run a definite course and get well of themselves, there are numerous plans of treatment for whooping-cough, and numerous remedies have from time to time been recommended by different men. These remedies have had for themselves longer or shorter periods of popularity, and many are forgotten. The literature of this subject is very large. It is unfortunate that many forms of treatment are recommended and become popular on insufficient foundation—a small number of cases reported, general impressions without careful record of cases, and lastly, disregard of the fact that the disease tends to recovery untreated.

Another source of error lies in the fact that whooping-cough varies very greatly in its severity, some cases even without treatment running a mild course with but few daily paroxysms. This variability is not taken into account, and it is very rare to find it stated at what stage treatment was begun. It is evident that there is a time in every case of whooping-cough when the administration of any drug will give apparently favorable results, simply because the disease is improving of itself. This natural improvement is sometimes very rapid without any treatment.

As the disease is a long and debilitating one it is plain that all drugs that interfere with the appetite, that disturb the digestion, or that depress the heart should be carefully avoided. It is far better to depend on hygienic treatment alone than to do harm in these ways, and render the patient more liable to complications.

The patient should be placed under the most favorable hygienic conditions, particular attention being given to good ventilation when the child is in the house. In favorable weather the patient should be out of doors as much as possible, and arrangements should be made, if possible, in summer for the child to sleep either in a tent or on a piazza or balcony. The diminution in the number of paroxysms while the child is in the open air is always very marked. The bedroom windows should be widely opened, the patient protected by screens from draughts, and an open fire kept going in the room if the weather is cold.

Sea-bathing, with care and moderation, in certain cases, or salt baths in the room, are of value, if they are followed by a warm and pleasant reaction of the skin. This reaction will be aided by rubbing the skin with a coarse towel. A change from the city to the country or seashore is often useful, but the danger of imparting the disease to others, and starting an epidemic in a new place, should always be considered. A mild moist atmosphere, by acting favorably on the laryngeal and bronchial inflammation, mitigates the disease. This can be obtained artificially by means of an atomizer, steam spray, or steam kettle, or by wet cloths hung about the room.

The diet should be carefully attended to; it should be very nourishing and easily digestible, and, if there is a tendency to vomit, food should be given frequently and in small quantities. The times of feeding should be arranged with reference to the paroxysms; thus, as

cough and vomiting are apt to occur in the morning on waking, it is better to wait for an hour or so till this has passed. At evening the child not infrequently has a paroxysm as soon as he is put to bed; hence, supper should be given at least an hour before bedtime, so that it will have a chance to be digested and not vomited. During the day food should be given after a paroxysm of coughing and vomiting, with the hope that it will be digested before the next attack.

The severity of the paroxysms may be mitigated by turning the child on its face with the head low, and detaching the mucus from the mouth with the finger, a practice which is commonly followed among the lower classes. The pressure of the hand over the eyes gives relief by preventing the strain upon them.

The number of drugs used is legion, and it is necessary to speak here of only the more important. Belladonna is one of the more popular antispasmodic drugs. It diminishes not only the hyperæsthesia and muscular spasm, but also the hypersecretion of mucus in the air passages. It is generally well borne by children, and should be given first in small doses, the dose being gradually increased till physiological effects appear. The medicine may then be given in smaller doses or omitted for a while. It is often given combined with the bromides.

Cocaine, from its marked local anæsthetic effect on mucous membranes, has naturally been used in the treatment of whooping-cough. It has been applied in solution by a brush to the larynx and pharynx, or sprayed into the throat by an atomizer, or by inhalation of its vapor. Cocaine should, however, be used with great caution and in very weak solution. Alarming symptoms have resulted from a few sprayings with a four-per-cent. solution in infants.

Cochineal and grindelia robusta have had reputations, and are still believed in by some. Dried chestnut leaves steeped in the form of a tea can be given safely to young children, and often appear to give surprisingly good results.

Antiseptic drugs are given internally by the mouth or rectum in whooping-cough, or applied locally by means of inhalation of atomized solutions or of gases; by applications of solutions to the pharynx, larynx, or nose, by means of brushes or swabs; by applications to the nose and pharynx by syringing; or, lastly, by the insufflation of fine powders into the nose, pharynx, or larynx.

One of the oldest forms of antiseptic treatment is the breathing of the air in the purifying room of gas-houses, a method, according to Roger, first used by Dr. Desmartes in 1859. Five or six years after this, this method became very popular, but it is at the present time but little used.

Among volatile antiseptic drugs given by inhalation may be mentioned turpentine, eucalyptus, pinus sylvestris, cresolin, thymol, and carbolic acid. These may be poured on boiling water, and the head held over the vessel, or they may be evaporated on water boiling over a lamp in a room. The objection to this method is that it is apt to interfere with free ventilation. Cases of poisoning from carbolic acid and cresolin have been reported.

Mohn has reported cases of whooping-cough cured, "as if by enchantment," by the use of sulphur fumigations. The child is dressed in clean clothes and sent from its room, which is closed and fumigated with burning sulphur for five hours in the morning. After the room is aired, the child sleeps there at night. One trial is generally sufficient for a cure. These observations have been confirmed by some and found valueless by others.

Quinine is deserving of more extended notice and its beneficial results were summed up in the Medical Congress of 1887 by Binz as follows:

First. That whooping-cough can be shortened and made mild by quinine (giving as many decigrams in twenty-four hours as the child has years).

Second. The prognosis is more favorable the earlier the treatment is begun.

Third. That the hydrochlorate of quinine given by the mouth is the best, the sulphate of quinine the next best form.

Laryngeal insufflations of quinine in the form of a fine powder were first used by Letzerich, one of the earliest investigators of the parasitic origin of whooping-cough, and the results reported by him and other observers have been very satisfactory.

Nasal insufflations of quinine have the advantage of greater simplicity of manipulation, and can easily be given by the parents—a very important consideration, for in a large class of patients daily visits of the physician in whooping-cough are out of the question. They are also less disagreeable to the patient, in fact can be given without in the least disturbing him.

Powdered benzoin, boric acid alone or mixed with roasted coffee, iodoform, tannin, and sal. ylic acid have also been used in nasal insufflations.

Resorcin is a drug which has been largely used by Dr. Moncorvo, of Rio Janeiro, in the treatment of this disease, and reference is here made to his important and elaborate monograph on the subject. He applies a one- or two-per-cent. aqueous solution of the drug with a brush or probang to the opening of the glottis daily, and with good results. The advantages of resorcin over many other antiseptics are its slight or agreeable taste, almost no odor, and its feeble toxic or caustic action. Moncorvo says that children object to the first application, but afterward submit with great docility.

Asaprol in a one-per-cent. solution applied to the larynx has been favorably reported, as has also a spray of peroxide of hydrogen 1 part, water 10 parts, and glycerin 1.5 parts. Menthol in liquid vaseline has also been used. The objection to all sprays and applications to the larynx is the difficulty of carrying them out in children and the liability to bring on gagging and vomiting.

Oxygen and ozone have also been used as inhalations.

Antipyrin has been used very largely in whooping-cough, notwithstanding its well-known depressant effects, and favorable results are reported by several able observers. Cases of injury from cardiac depression are also recorded, and it seems doubtful whether it is well to run the risk of the unfavorable effects of this drug.

Bromoform has been largely used of late, and appears to act better than most other drugs in diminishing the frequency and the severity of the paroxysms of whooping-cough. It should never be given in an emulsion, as, unless the bottle is thoroughly shaken, it will settle to the bottom and the last few doses cause serious or fatal results. It is best dropped on sugar, the dose being about one drop for each year of age, given every four hours.

Another still more recent drug of great value in whooping-cough is heroin. This can be given to a child three years old in doses of gr. $\frac{1}{3}$ three or four times daily, and it certainly has considerable effect in quieting the paroxysms, although in some cases it is of but little value.

Of late, various compounds with suggestive names have been used with varying success. The interpretation of these names follows:

Antitussin = difluorphenyl.

Pertussin = saccharated extract of thyme.

Antispasmin = a combination of one molecule of narcein natrium with three of salicylate of sodium.

Tussol = amygdalic acid and antipyrin.

Prophylaxis.—The only means we have for the prevention of the spread of whooping-cough is isolation of the patient.

Isolation in the case of the exanthemata is easily practised on account of the short duration of these diseases, and the fact that the patient is confined to bed. In whooping-cough, however, we have a disease whose period of contagiousness may continue over two months, during which the patient is able to be about the house and go out of doors. It is a disease which is usually not recognized, and for which the physician is not called till a week or two have elapsed, during which the other members of the household, and probably of the school, are exposed to contagion. Hence isolation is rarely prac-

tised, and mothers among certain classes even adopt the pernicious practice of allowing their children to be exposed to contagion, on the ground that they must have whooping-cough some time, and the sooner they have it and are over it the better. This idea should be combated wherever found, for, as we have already seen, the older a child is the better able is he to resist the debilitating effects of the disease, while in infants the danger of a fatal result is considerable. Adults, even if not less susceptible, are less frequently exposed to whooping-cough than young children, and in them the disease generally runs a mild course. If possible, the patient should live and sleep in a room away from the other children of the family, who should not be allowed to visit him or play with him out of doors. The mother or nurse should, if possible, air or change her clothes and wash her hands on leaving the patient to go to the other children. These precautions are certainly worth while if there be a young infant in the family, or a delicate child, or one weakened by sickness.

Parents should be reminded of the evil of taking children suffering from this disease in public conveyances, or to places of public meeting, as churches, shops, where other children may be infected.

Dispensaries and out-patient departments of hospitals often serve to spread the disease, the child with whooping-cough sitting, perhaps for several hours, on benches with other children. Such cases should either be seen and sent off at once, or kept in a separate room.

It is unfortunate that whooping-cough should be especially contagious in the early stages before the diagnosis is made clear by the characteristic whoop. The contagion diminishes during the spasmodic stage and probably ceases before the child has ceased whooping.

Disinfection of the room and its contents, after death or recovery from whooping-cough, should always be practised, although, as before remarked, it is not probable that the poison survives long outside of the body.

Charles W. Townsend.

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WIDAL TEST. See *Typhoid Fever.*

WIESEN. See *Dacos.*

WILBUR SPRINGS.—Colusa County, California.

These mineral springs are located thirty miles from Colusa. They are pleasantly situated and have acquired considerable reputation. The waters are hot and sulphureted, and, according to Anderson's analysis, one United States gallon contains (solids): Sodium chloride, gr. 19.75; sodium carbonate, gr. 3.40; sodium sulphate, gr. 26.19; potassium chloride, gr. 0.46; silicates, gr. 6.95; magnesium sulphate, gr. 22.90; magnesium carbonate, gr. 5.10; calcium carbonate, gr. 8.44; calcium sulphate, gr. 20.62; ferrous sulphate, gr. 4.16; alumina, gr. 3.93; potassium iodide, gr. 0.75; organic matter, gr. 1.74. Total solids, 124.39 grains. Sulphureted hydrogen gas, 43.97 cubic inches. A hotel and cottages have been built, and there are also excellent camping facilities.

James K. Crook.

WILDEN SPRING.—Franklin County, Vermont.

Post-Office.—St. Albans. Hotel in St. Albans.

Access.—St. Albans is a prominent railroad station on the Vermont Central Railroad, in the extreme north corner of the State.

St. Albans is a delightful town overlooking Lake Champlain, two miles west. The spring is situated on Edwards Street, south of Lake Street, about ten minutes' walk west of the depot. The water was analyzed by A. A. Hayes, M.D., of Boston, who found the following chemical constituents: Sodium carbonate, magnesium carbonate, calcium carbonate, sodium chloride, potassium sulphate, calcium sulphate, magnesium iodide, iron crenate, sodium silicate. Solid constituents per United States gallon about twenty-four grains.

The water has been considerably resorted to in the past, but so far as we can learn it is not now employed for medicinal purposes. *James K. Crook.*

WILHOIT'S SODA SPRINGS.—Clackamus County, Oregon.

Post-Office.—Wilhoit. Hotel.

Access.—From Salem, Marion County, twenty-five miles northeast by wagon road.

These springs are seven in number and flow about seven hundred gallons per hour. An analysis by J. A. Veatch, M.D., in 1869, gave the following results: One United States gallon contains (solids): Sodium carbonate, gr. 87.57; magnesium carbonate, gr. 85.32; calcium carbonate, gr. 32.23; iron carbonate, gr. 6; sodium sulphate, gr. 3.40; magnesium sulphate, gr. 6.45; sodium chloride, gr. 201; iodine, a trace. Total solids, 421.97 grains. Carbonic acid gas, 22.56 cubic inches.

The water, as it flows, is said to have a temperature of 35° F. This is a very valuable water, combining as it does a number of important chemical ingredients. It is not unpleasant to the palate, and, according to Dr. H. Carpenter, it operates on the second day as a laxative and diuretic. It contains a considerable percentage of iron, which gives it tonic and reconstructive properties.

James K. Crook.

WILLOW. See *Salicaceæ.*

WINNIPEG.—This city, the capital of the province of Manitoba, is situated at the junction of the Red River of the North and the Assiniboine, 485 miles south of Lake Winnipeg and 1,424 miles west of Montreal. From the boundary of the United States it is about 60 miles north, North Dakota and Minnesota forming the southern boundary of the province. It is a city of 45,000 inhabitants, the metropolis of all this region, and is constantly growing. It is well laid out with broad streets, and has many public buildings—colleges, handsome churches, a general hospital, banks, etc. It is reached viâ the Canadian Pacific Railroad from the east, or the Northern Pacific from St. Paul.

The province of Manitoba, embracing 73,956 square miles, is a level prairie, about 800 feet above the sea-level, and contains three important lakes: Winnipeg, Manitoba, and Winnipegoosis. Like the neighboring Dakotas and Minnesota, Manitoba is noted for its wheat, which is the staple product. The rivers and lakes abound in fish, and large and small game is plentiful.

The climate of this region is healthy, but the extremes of temperature are great, as is also the annual range. The winters are long and cold. According to Hann ("Handbuch der Klimatologie") the temperature falls almost every winter as low as 40° below zero F., while in summer it may rise to 100° F. Owing to the comparative dryness of the air, however, the cold is said not to be severely felt. The average annual mean temperature of Winnipeg is 33.8° F., which, according to Hinsdale, is lower than that of any other large city in America.

The following table of the monthly and annual temperature and precipitation was kindly furnished by Prof. R. F. Stupart, director of the Meteorological Service, Toronto:

WINNIPEG, MANITOBA

Table showing	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Year.
Average mean highest temperature	5.4°	10.4°	24.6	46.6°	65.1°	74.5°	78.3°	75.9°	64.7°	50.2°	27.8°	14.6°	78.3°
Average mean lowest temperature	−16.2	−12.6	7.4	25.3	39.0	49.7	53.8	50.5	41.0	28.4	10.0	−5.3	−16.2
Average mean monthly and annual temperature	−5.4	−1.1	16.2	36.0	52.1	62.1	66.1	63.2	52.8	39.7	18.9	4.6	33.8
Average daily range of temperature	21.6	23.0	16.7	21.3	26.1	24.8	24.5	25.4	23.7	20.9	17.8	19.9	....
Absolute highest temperature	40.0	46.0	54.0	90.0	94.0	96.0	98.0	103.0	94.0	85.0	64.0	47.0	103.0
Absolute lowest temperature	−46.0	−46.0	−38.0	−14.0	15.0	21.0	36.0	30.0	19.0	−3.0	−34.0	−53.0	−53.0
Average rainfall in inches	....	....	0.25	1.17	2.15	3.53	3.08	2.63	2.09	1.52	.17	.14	16.73
Average snowfall in inches	8.7	9.1	8.8	4.3	1.3	.3	....	....	....	1.3	9.8	7.6	51.5

The average daily maximum temperature for July is 78.3° F., and the minimum, 53.8° F. The annual range of temperature is from 130° to 140° F. The average total annual precipitation for Manitoba is 17.43 inches, but of this 12.87 inches falls in the six months from April 1st to October 1st. The mean relative humidity is about seventy-five per cent. The wind velocity is very considerable, averaging about eleven miles per hour, the prevailing direction being from the north and northwest.

The most notable features, then, of the climate of this region are the great extremes of temperature, the great daily and monthly ranges, and the excessive cold of winter. From the fact, however, that spring rapidly advances during the latter part of April, and that the day temperatures in summer are high, with a good deal of sunshine, the wheat matures quickly. There is no malaria, and, as has been said, the climate is a wholesome one for the robust, and immigration is rapidly filling up this great fertile region. *Edward O. Otis.*

WINTERGREEN.—(*Gaultheria;* Checkerberry; Boxberry; Partridge-berry; Tea-berry, etc.)

The dried leaves of *Gaultheria procumbens* L. (fam. *Ericaceæ*). This plant is a little evergreen undershrub, with slender, weak, creeping or subterranean stems, and at intervals ascending or erect; branches from two to four inches high, each bearing three or four leaves and a few axillary, nodding flowers; leaves oval or obovate, thick, leathery, almost entire, bright-green and shining above, paler beneath, with slightly revolute margins, fragrant when crushed, and pleasantly aromatic to the taste. Flowers small, calyx five-toothed, enclosing the small capsule, becoming fleshy as it ripens, and forming the principal portion of the pleasant-flavored fruit. Corolla ovoid, five-toothed; stamens, ten; pistil, one, with five-celled ovary; pod, five-celled, many-seeded, surrounded by the juicy calyx. The berry, which is edible and occasionally found in the markets, is about a fourth of an inch in diameter, pink or red in color, of a sweetish, aromatic, birch-like taste.

FIG. 5037.—Wintergreen; Leaves and Berries. (Baillon.)

Gaultheria is a native of North America, growing in dry woods and plains. It is in many parts of the United States very abundant, carpeting the ground under trees and bushes, and is collected in large quantities both for use, dried, and for immediate distillation. All parts are aromatic, the leaves and stems astringent as well, and owe their value to an essential oil (*Oleum Gaultheriæ*, U. S. P.) of birch-like flavor, consisting mostly of *methyl salicylate*, with about one-tenth of a peculiar hydrocarbon, *gaultherilene*. Oil of wintergreen is "a colorless, yellow or reddish liquid (according to age), of a peculiar strong and aromatic odor, a sweetish, warm, and aromatic taste, and a slightly acid reaction. Specific gravity about 1.180. It is readily soluble in alcohol."

Like sassafras, cinnamon, and other pleasant aromatics, wintergreen is very largely used as a flavor, and enters into several official preparations for that purpose. Its relation to salicylic acid has led to its employment in rheumatism. The discussion is very animated as to whether oil of wintergreen, oil of birch, and pure methyl salicylate are identical in physiological action. By many the natural oil of wintergreen is preferred to either of the others. Dose of the leaves, 1–4 gm. (gr. xv.–lx.); of the oil, from five to twenty drops.

Preparations: Of the oil, spirit (*Spiritus Gaultheriæ*, U. S. P.) 0.05 in alcohol. *W. P. Bolles.*

WITCHHAZEL.—(*Hamamelis*, U. S. P.) The dried leaves of *Hamamelis Virginiana* L. (fam. *Hamamelidaceæ*). The plant yielding this drug is a tall, slender, straggling shrub growing commonly, in moist woods, over a large part of the United States. Its flowers are small, in little, sessile, axillary clusters, and appear late in the autumn. They persist through most of the winter, the fruit from them ripening in the following summer. Calyx four-parted; corolla of four long, narrow, strap-shaped, yellow petals; stamens, eight, short; pistil, one, with two styles; and a two-celled, two-ovuled ovary.

The leaves should be collected in the autumn. They are stoutly and very shortly petioled, the blade 7–15 cm. (3–6 in.) long and nearly as broad or occasionally even broader, highly inequilateral, oval, with a very oblique, slightly cordate base, and usually a very short obtusish point at the summit, the margin coarsely sinuate; thickish, dull green and with obscure venation above, paler or brownish-green, with a satiny lustre and very prominent

principal veins underneath, nearly smooth, the few hairs of the lower surface having much thickened walls and a very small lumen; odor rather faint, characteristic; taste astringent, slightly aromatic bitter.

A number of analyses of this plant have been made without discovering anything to explain its reputed vir-

FIG. 5038. Witchhazel; Flowering Branch. (Baillon.)

tues. It is not poisonous in any quantity. There is some *tannin*, and an infinitesimal amount of *essential oil*; enough to give smell and taste to a distillate, but scarcely enough to isolate.

It is an old remedy of the Indians, and is said to have been introduced to our notice by them; but its present popularity as a wash for bruises and wounds in household practice is of very modern growth.

For twenty years or so it has been, in this country, the most widely used domestic vulnerary, taking the place in the popular estimation of arnica, which had held sway for a generation before. It is usually employed in the form of a distillate, made by distilling a very weak mixture of alcohol and water (six-per-cent. alcohol). It has an odor and faint taste derived from the drug, but not enough oil or extract to be estimated in any other way. The odor is pleasant and suggestive of liniment, and the preparation is on the whole a fair evaporating lotion. A fluid extract (*Extractum Hamamelidis Fluidum*) is official, and contains, besides the fragrant principles, considerable

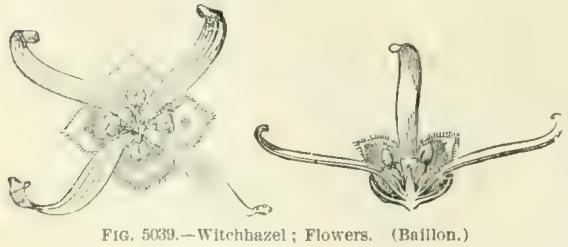

FIG. 5039.—Witchhazel; Flowers. (Baillon.)

tannin, which the distilled preparation of course does not. It may be diluted for washes, vaginal douches, etc. Witchhazel at present is rarely given internally.

The bark is similarly employed, and much of the distillate is said to be prepared from it. It is regarded by many as being superior to the leaves.

Henry H. Rusby.

WITTER'S MINERAL SPRING.—Lake County, California

These springs are pleasantly located about one mile east of Pearson's Springs, five miles from Upper Lake, and three miles from Blue Lake. The altitude is 1,800 feet. The resort is a growing one, and is very picturesquely located, having excellent views of the lakes, valleys, and mountains in the vicinity. There are a good hotel, several cottages, and fine bathing facilities for hot and cold mineral baths. The springs are all cold and flow about sixty gallons an hour. There are cold soda and iron springs, and cold sulphur springs. The principal spring is composed as follows: One United States gallon contains (solids): Sodium chloride, gr. 17.42; sodium carbonate, gr. 5.96; sodium sulphate, gr. 11.50; potassium carbonate, gr. 3.15; magnesium carbonate, gr. 7.10; magnesium sulphate, gr. 20.62; ferrous carbonate, gr. 1.17; manganese carbonate, gr. 0.86; alumina, gr. 1.65; borates, gr. 0.42; silica, gr. 6.33; organic matter, gr. 0.76; total solids, 76.94 grains. Carbonic acid gas, 7.65 cub. in.; sulphureted hydrogen, 5.25 cub. in. Temperature of water, 59.3° F.

This spring has received the very emphatic if not euphonious title of Dead Shot Spring, having reference to the action of the water on the diseases for which it is recommended. The water is said to be highly efficacious in liver, kidney, and bowel disorders.

James K. Crook.

WOLFER'S MINERAL SPRING.—Marion County, Oregon.

POST-OFFICE.—Hubbard. Hotels.

ACCESS.—Viâ Southern Pacific Railroad to Hubbard, thirty-one miles from Portland and twenty miles from Salem. The spring is within five minutes' walk of the depot.

This spring is mentioned as "Lehman's Spring" in the Geological Reports for 1895. Hubbard is situated in the Willamette valley, in the midst of a fine fruit and garden country. The spring (artesian) is located on the hillside, at a level of 212 feet above the sea. It is surrounded by an arbor of wild willows, and forces its way to a height of four feet above the surface, forming a beautiful fountain. It yields about six thousand gallons of water per hour. There are beautiful grounds about the springs, well adapted for outdoor sports, picnics, etc. According to a partial analysis by Professor Fisk, the water contains: Calcium carbonate, magnesium carbonate, sodium chloride, potassium chloride, iron oxide, silica, and alumina. The water is said to possess valuable properties as a tonic and laxative. *James K. Crook.*

WOOD-TICK. See *Arachnida*.

WOOL-SORTERS' DISEASE. See *Anthrax*, and *Occupation, Hygiene of*.

WOOTAN WELLS.—Robertson County, Texas.

POST-OFFICE.—Wootan Wells. Hotel and cottages.

ACCESS.—Viâ Houston and Texas Central Railroad to Wootan Junction; thence two miles to springs. Street cars meet all trains, day and night, from about April 1st to November 1st; during the winter months there are only day trains.

The location is 145 miles north of Houston, and 125 miles south of Dallas. These wells are located on a picturesque eminence about 500 feet above the level of the gulf. The first well was dug in 1877 by Mr. F. M. Wootan, an emigrant from Alabama. The water was found to be useful for cooking or washing purposes, so Mr. Wootan rented the farm on which the well was situated to a neighbor, whose health was bad and who also had a puny wife and children. They found it necessary to use the "bad" water for drinking purposes, and the sickly family all got well and remained well. This was the beginning of a health resort which has now become widely and favorably known. Persons with means became interested. More wells were dug, and at this time about all the attractions of any first-class interior watering place will be found here. These include a large, well-arranged brick hotel, with abundant bathing facilities, an opera house, archery court, croquet grounds, beautiful groves, camp grounds, etc. The place is naturally well adapted for good drainage, and no pains

are spared by the management to keep the surroundings in a sanitary condition. The resort is open the year round. Analyses of the different wells show very little difference in their chemical ingredients. Following are specimen analyses of two of the wells, the first by Prof. Charles F. Chandler, of New York, and the second by Dr. W. M. Mew, chemist of the United States Naval Department, Washington, D. C.:

Well No. 1.—One United States gallon contains (solids): Chlorides, gr. 23.34; magnesium, gr. 13.11; calcium, gr. 25.21; iron protoxide, gr. 1.20; iron sesquioxide, gr. 0.69; aluminum sesquioxide, gr. 1.22; manganese oxide, gr. 0.54; sulphates, gr. 59.67; silica, gr. 3.28; organic and volatile matter, gr. 9.62. Total solids, 137.88 grains.

Well No. 4.—One United States gallon contains (solids): Chlorides, gr. 36.36; magnesium, gr. 22.75; calcium, gr. 28.18; iron sesquioxide, gr. 13.06; aluminum sesquioxide, gr. 3.45; manganese oxide, gr. 0.57; sulphates, gr. 86.41; sodium, gr. 18.10; silica, gr. 4.69. Total solids, 213.57 grains.

These waters show about the same general characteristics, No. 4 being somewhat richer in mineral ingredients, especially in iron, than No. 1. It will be observed that the chemists have not worked out in full the combinations of the various elements present. There can be no doubt, however, that the most important compounds contained in the waters are the sulphates of magnesia and soda, and probably the sulphate of iron. These ingredients should impart, in the proportions here probably present, mild cathartic properties, and, in No. 4 especially, the effects of a strong ferruginous tonic and blood restorer. The waters are highly prized by Texas physicians in the treatment of the various forms of nephritis and in diabetes and rheumatism. They are of undoubted efficacy in some cases of dyspepsia and in catarrhal jaundice and other disorders of the liver and alimentary tract. The water is used commercially, and is shipped to various parts of the United States. *James K. Crook.*

WORMSEED, AMERICAN.—(*Chenopodium*, U. S. P.; *Ansérine vermifuge*, Codex Med.) The dried ripe fruit of *Chenopodium ambrosioides* L. or of *C. anthelminticum* L. (fam. *Chenopodiaceæ*).

The first-named species is the old-fashioned garden plant *Mexican tea* or *Ambrosia*, native of tropical America; the second appears to be of European nativity. Both are common weeds in the Eastern United States, growing along roadsides, about wharves, lumber yards, etc., and are of a sprawling and ascending habit, reaching a height of two or three feet. They have a strong, heavy odor, disagreeable to most people. The fruits, generally called "seeds," are nearly $\frac{1}{12}$ of an inch (2 mm.) in diameter, depressed, globular, glandular, dull-greenish or brownish, the integuments friable, containing a lenticular, obtusely edged, glossy, black seed. This seed has a peculiar, somewhat terebinthinate odor, and a bitterish, pungent taste.

The fruits contain one or two per cent. of a rather disagreeable, minty, essential oil, which represents it medicinally. This oil is usually distilled from the entire herb. It is a thin, and, when fresh, colorless liquid of aromatic odor and bitterish taste; specific gravity, 0.920.

Like most aromatic herbs, chenopodium, in small doses, is a stomachic tonic; in large doses it is irritating and nauseating. The property for which it is mostly prized is, however, its poisonous action upon intestinal worms, particularly upon the lumbrici. From five to fifteen drops of the oil in emulsion or on sugar is the usual range of doses. Oil of Chenopodium is a very powerful poison in overdoses. The symptoms are chiefly referable to intestinal irritation and cerebral congestion. There are drowsiness, great thirst, abdominal pain, perhaps with vomiting, intense sensitiveness to light and sound, but with indistinctness, aphasia of both kinds, stupor, coma, and death. The treatment is stomach evacuation, purging, with watery stools, free administration of water, enemata, brandy, and external heat.

W. P. Bolles.

WORMSEED, LEVANT.—(*Santonicum*, U. S. P.; *Flores Cinæ*, P. G.; *Flores Artemisiæ Semen Contra Semen tum.*) The dried unexpanded flower-heads of *Artemisia pauciflora* (Ledeb.) Weber (fam. *Compositæ*). Although the plant yielding these flower-heads is well known, there is great difference of opinion among botanists as to its specific reference. By many it is regarded as a variety of *A. maritima* L. of Southern Europe. The German Pharmacopœia still refers the drug to *A. Cina* Berg. The drug is collected in the Turkestan deserts, and most of it, and the best, is at once consumed there in the manufacture of santonin, the percentage of santonica exported being steadily on the decrease. Several related and similar, but hairy products have occasionally been imported from India and Africa, and chenopodium is occasionally sold for it. The drug is also subject, through imperfect cleaning, to the presence of pieces of branchlets and leaves, and dirt of various kinds; yet it is usually clean and of fine quality. It deteriorates readily on being kept, especially if not carefully protected in a closed and dark container. In proportion as the greenish-gray tinge has changed to a brown, it may be regarded as having thus deteriorated. The drug is thus described:

A yellowish-green (at length greenish-brown) somewhat glossy, mobile mass; having a strong and peculiar, somewhat camphoraceous odor and an aromatic and bitter taste; heads 2–4 mm. ($\frac{1}{12}$–$\frac{1}{6}$ in.) long, oblong-ovoid, slightly flattened, obtuse, consisting of an involucre of about twelve to eighteen closely imbricated, glandular scales with broad midribs, enclosing four or five rudimentary florets.

With gum, a little resin, and ordinary plant constituents, three specific bodies exist in santonica. Its one and one-half to two per cent. of volatile oil consists chiefly of cineol, and is somewhat like oil of eucalyptus in properties. Santonin, of which there is usually not more than two per cent., as the drug occurs here, is the active anthelmintic agent and is described under that title. A small and variable amount of artemisin occurs, obviously resulting from the oxidation of santonin.

Although santonica possesses, in correspondingly lower degree, the anthelmintic properties of santonin, the latter alone is used for that purpose. As an aromatic bitter, santonica is occasionally used in doses of 0.3–2 gm. (gr. v.–xxx.). There is no official preparation.

Henry H. Rusby.

WORMSEED, POISONING BY. — *Chenopodium ambrosioides* L.; and *C. anthelminticum* Gray, which are possibly only varieties of one species, contain a volatile oil which has a strong, disagreeable odor, and decided vermifuge properties. It is most abundant in the seeds. It is somewhat analogous in composition to oil of turpentine. By keeping it undergoes oxidation, and probably other changes. The seeds of the plant are used as a remedy for intestinal round worms and are often given to children as a domestic remedy. Little harm appears to result from this practice, but the use of the oil itself has led to fatal results in several cases. One of the earliest of the American cases to be fully reported was that by Dr. Brown in the *Maryland Medical Journal* in 1878. A man, aged thirty-one years, was supposed to have taken over an ounce of the oil, purposely substituted by him for castor oil. He suffered from nausea, later with severe vomiting, dizziness, buzzing in the ears, diminished sensitiveness to some sounds and hypersensitiveness to other sounds. Still later, marked aphasia and confusion of ideas occurred. He died five days after the material was thought to have been taken. He was, however, a confirmed self-drugger, and deceived the attending physician throughout the whole history of his illness, denying that he had taken the oil, though the odor of it was unmistakable. Another case was that of a child, aged two years, to whom was given one teaspoonful of the oil. The immediate symptoms were deep sleep, clammy skin, and muscular weakness. Brandy and milk were given. The patient became restless and was quieted with bromides. She became somewhat bet-

ter, but then became worse, could not stand up or walk alone, and vomited material which had the odor of the oil. Her hearing was for a while affected. She recovered.

In another case a boy, aged three years, was given a teaspoonful of the oil. He vomited and then went into a stupor. The pupils were small but equal; pulse, respiration, and temperature normal. Salt water was given as an emetic, then one grain of calomel, and repeated doses of castor oil. He became worse, developing deep stupor and twitching of the arms, and died. In another case a man, aged sixty-three years, died after taking, in divided doses during the course of a single day, one ounce of the oil. No direct antidotal treatment was employed. He was comatose.

The disturbance of hearing noticed in several of the cases is a remarkable feature, but has not been explained. It must be borne in mind that in some of the cases the amount taken and the exact nature of the material were not established. From the reports it appears that the oil is actively toxic, and that caution should be given in works on materia medica concerning its use. Very little is said upon this question in the standard works. Its effects seem to be both as an intestinal irritant and as a neurotic poison. The odor will probably afford the best means of making a diagnosis. No characteristic post-mortem changes are recorded.

Treatment will be difficult. Early and free evacuation of the stomach and bowels is important. Strong coffee might be useful. Irritating emetics are contraindicated.

Henry Leffmann.

WORMWOOD.—(*Absinthium*, Vermouth.) "The leaves and tops of *Artemisia Absinthium* L. (family *Compositæ*)," U. S. P. A half-shrubby plant, with numerous erect stems two to four feet high, grayish silky throughout. The leaves are nearly equally gray on both sides, twice or thrice pinnatifid, the divisions oblong and obtuse, the larger ones three or four times as long as broad. The small heads are short-peduncled, solitary, and cernuous in the axils of leafy bracts, and the floriferous branches are panicled. The characters of flowers and fruit will be found described under *Artemisia*. The odor is strongly aromatic and the flavor very bitter.

The plant is native to Asia and perhaps Europe, and has become extensively naturalized in nearly all temperate countries, and even in the tropics, at high altitudes.

The activity of absinthium depends upon the two constituents: *absinthol*, which constitutes the most of its one per cent. of volatile oil, and *absinthin*, a bitter glucoside, soluble in both alcohol and water. In its volatile oil occurs also the blue oil of chamomile flowers. Oil of wormwood is an important commercial article, being largely in demand in France for the manufacture of the alcoholic beverage *absinthe*. Tannin, resin, and succinic acid also occur in this drug. Absinthium is an aromatic bitter, acting like chamomile, especially as a gastric tonic. It is also mildly antiperiodic and anthelmintic. The oil has specific nervine properties, a dose of half an ounce having caused alarming symptoms, with convulsions and insensibility. An absinthe habit is formed by the continued use of the liquor, the victims suffering from neuralgia, muscular tremors, epilepsy, and impaired intellect. Observations have established the fact that these effects are due to the absinthium and not to the alcohol. The dose of the herb is 1–4 gm. (ʒ ¼–i.); of the oil, ♏ i.–iij. Large quantities of the oil would undoubtedly prove fatally poisonous.

Henry H. Rusby.

WRIST, JOINTS OF THE.—The skeleton of the wrist, being a series of small bones essentially similar in character, may be considered as a whole, and we may hence conceive a superior radiocarpal or wrist-joint proper, between the bones of the forearm and the carpus, and an inferior or carpometacarpal joint, between the carpus and the metacarpus. Again, we may consider separately the two rows of carpal bones, and regard the somewhat irregular union between them as an intracarpal or mediocarpal joint. Finally, we may consider each bone as a separate unit and its union with each of those which it touches as so many carpal joints of a secondary degree.

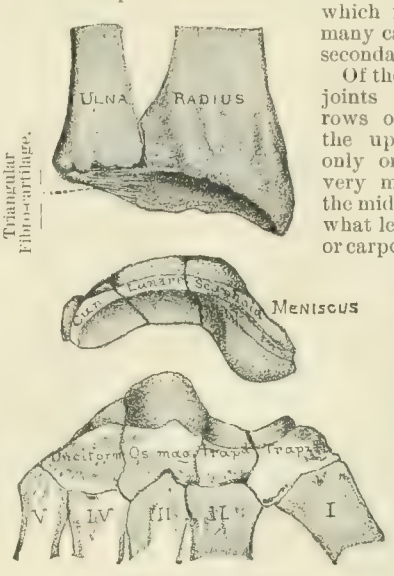

Fig. 5040. The Wrist-joints.

Of the three transverse joints formed by the rows of carpal bones, the upper one is the only one that has any very marked mobility, the middle one has somewhat less, and the lower or carpometacarpal joint has the least of all. It is, indeed, instructive and logical in regarding the movements to follow the plan adopted by Meyer, and consider the lower row of bones as combined for practical purposes with the metacarpal bones with which they articulate and the upper row as an articular integer or meniscus which is the essential interposed element between the forearm and the hand. Viewing the form of the surfaces, the articulation between the meniscus and the forearm is a pommel or ellipsoidal joint. Movement is necessarily freest in the direction of the

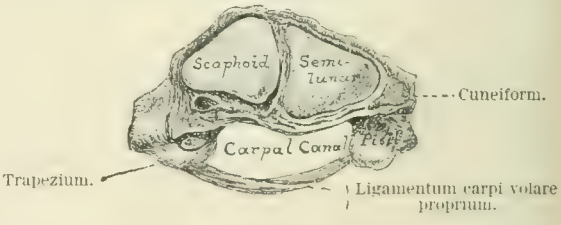

Fig. 5041.—The Carpal Canal.

ellipsoid, but still a certain amount of rotation is possible. The surfaces involved are those of the triangular cartilage and the radius above, and the scaphoid, semilunar, and cuneiform below. The ulna does not enter into the articulation, nor does the pisiform bone. Many comparative anatomists are of the opinion that the triangular

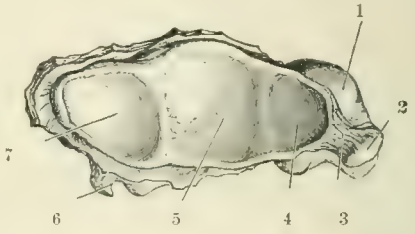

Fig. 5042.—Articular Surface of the Wrist-Joint. (Cunningham.) 1, Head of ulna; 2, styloid process of ulna; 3, apex of triangular fibro-cartilage; 4, triangular fibro-cartilage; 5, surface of semilunar bone; 6, groove for tendon of extensor longus pollicis muscle; 7, surface for scaphoid bone.

fibro-cartilage represents a carpal element which in its complete form long ago vanished from the mammalian carpus and that the pisiform bone is another vestige of the same kind. Certain facts of abnormal variation seem to support this view and to show that the pentadactylate

form of the human hand is not the primitive form firmly fixed though it now is, but that a seven digit hand was probably the original mammalian type. Odd cases of supernumerary wrist-bones and fingers, which are occasionally seen, are, according to this view, instances of atavism.

The midcarpal joint is of a mixed character, having, like the midtarsal joint of the foot, a wavy outline, the comparatively large, convex upper surfaces of the os magnum and unciform bones making together a sort of ball-like head which fits into the hollow socket made by the under surfaces of the combined scaphoid, semilunar, and cuneiform bones; while a comparatively small surface of the scaphoid articulates with the trapezium and trapezoid to make a curve in the opposite direction. This assists considerably in twisting movements of the hand, such as pronation and supination, which are very necessary to that nicety in the management of tools which characterizes the hand of man. The hand of the ape is by no means so delicately adjusted in this particular.

It has been well pointed out by Professor Humphrey, in his classical treatise on the "Human Skeleton," that the wrist owes the security of its joints, not so much to the interlocking shape of the joint surfaces, or to the strength of its ligaments, as to the strong tendons which pass over it, tend to protect it, and render it at the same time flexible. A short examination of the lower end of the radius will show that its dorsal aspect is deeply grooved for the extensor tendons which pass in every direction over the back of the hand. They are bound closely down in their grooves by a strong band of fascia called the posterior annular ligament, which thus becomes, as it were, one of the most powerful protecting ligaments of the radiocarpal joint. In a similar manner the anterior surface of the wrist is hollowed out by a deep archway, the carpal canal, so called because it is spread over by strong bands of fascia which confine the flexor tendons in a sort of subway.

English anatomists group these bands together indiscriminately as the anterior annular ligament, but there can readily be distinguished two bands—a superficial one, to which the name of annular ligament may properly be applied, as it is a process of the deep fascia of the

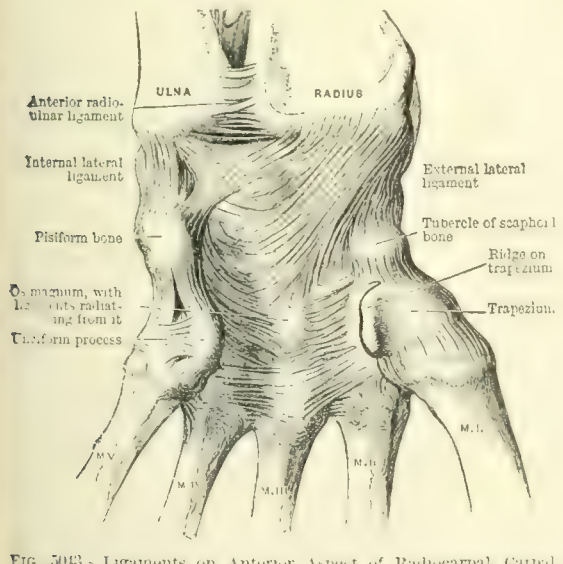

FIG. 5043.—Ligaments on Anterior Aspect of Radiocarpal, Carpal, and Carpometacarpal Joints. (Cunningham.)

arm which passes over the tendon of the palmaris longus and the ulnar vessels and nerve, being continuous with the posterior annular ligament at either side; the second is more independent, partaking more of the nature of a ligament, and therefore properly designated as the ligamentum carpi volare proprium. It is a strong, firm band, attached on either side to the carpal eminences—that is to say, the pisiform and unciform bones on the

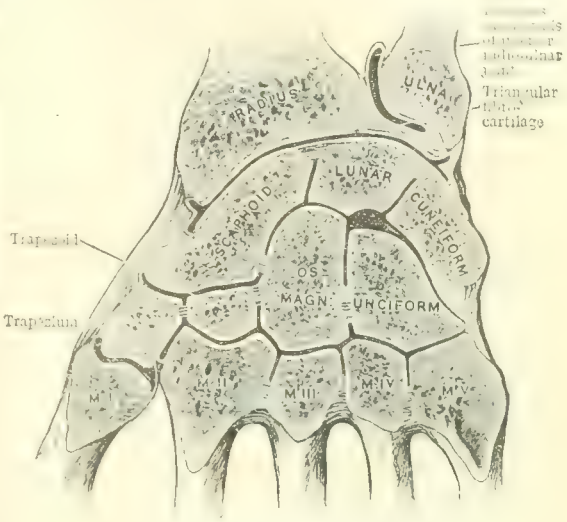

FIG. 5044.—Coronal Section through the Radiocarpal, Carpal, Carpometacarpal, and Intermetacarpal Joints, to show Joint Cavities and Interosseous Ligaments (diagrammatic). (Cunningham.)

inner side and the tubercle of the scaphoid and the ridge of the trapezium on the outer side. It passes *under* the tendon of the palmaris longus and the ulnar vessels and nerve. Beneath it pass the great flexor tendons and the median nerve, confined by several strong sheaths which blend with each other and send fascial processes to the ligament above and the attachments of the special bones below. It is to this arrangement, combined with pronation, that we owe the surprising flexibility which characterizes the wrist, a flexibility which permits the extraordinary twists so famous in the pitching of a ball, the handling of a tennis racket, and the parrying of the thrust of a foil.

Viewing the wrist-joint with reference to its synovial cavities, we find that the radiocarpal joint has its own cavity, the midcarpal and carpometacarpal having a common cavity, there being excluded two bones, the pisiform and the metacarpal bone of the thumb, each of which has its own special articulation—the first with the cuneiform, the second with the trapezium.

The intrinsic ligaments of the carpus are of two classes: one being external strengthening bands, the others internal, interosseous, serving as close interties to keep the whole system firm. On the palmar surface a somewhat irregular mass of fibres, stretching from the bones of the forearm to the metacarpal bones, has received the name of the ligamentum carpi volare profundum.

Separate portions of this have received different names. Thus the arcuate ligament is that portion which passes downward and inward from the radius to the cuneiform bone; the straight ligament (ligamentum carpi rectum) is a rounded fasciculus that passes from the styloid process of the ulna to the semilunar and cuneiform bones, and the funiculus ligamentosus a similar one extending from the same to the cuneiform and pisiform bones. Bands from the pisiform bone to the unciform and to the fifth metacarpal (ligamentum piso-hamatum, ligamentum piso-metacarpeum) are regarded as extensions of the insertion of the flexor carpi ulnaris. A series of short bands connecting the os magnum with the contiguous bones is known as the radiate ligament. Finally, the most distal band, connecting the bases of the metacarpal bones, is known as the deep transverse ligament. All these divisions seem hardly necessary.

The investment on the dorsal surface is not usually so complete. The strengthening bands are mainly two—the rhomboid ligament, passing downward and inward from the lower end of the radius to the cuneiform and unciform bones, and the transverse dorsal ligament, extending from the scaphoid outward to the same. There is also a dorsal radiate ligament diverging from the os magnum.

The only other joint requiring especial mention is that of the metacarpal bone of the thumb with the trapezium. This is an excellent example of the joint by reciprocal reception, sometimes termed the saddle-joint. Its motions are freest in two directions, which correspond to the motions of adduction and abduction on the one hand, and of the various adjustments of opposition on the other.

Frank Baker.

WRIST-DROP. See *Lead Palsy.*

WRITERS' CRAMP. See *Hands and Fingers, etc.*

WRY-NECK. See *Torticollis.*

XANOL is sodium caffeine salicylate, a diuretic of considerable power, with very little of the caffeine effect on heart and nervous system. Dose, 0.3–1 gm. (gr. v.–xv.).

W. A. Bastedo.

XANTHELASMA, XANTHOMA. See *Eye, Tumors of.*

XANTHORRHŒA RESIN.—*Resina lutea; Acaroides Gum* or *Resin; Botany Bay Gum* or *Resin.* By these names are designated several closely related solid balsams, obtained in Australia from species of *Xanthorrhœa* (fam. *Liliaceæ*).

The resinous sap exudes spontaneously, and hardens upon the stem in tears or masses. Two principal varieties of the "gum" are distinguished: the red, in deep red lumps or fragments resembling lumpy specimens of dragon's blood, having a weak odor of benzoin, and a spicy cinnamon-like taste; the yellow, in orange-yellow pieces or tears, having a strong benzoin odor.

The balsam contains, besides some bassorin and uninteresting ingredients, a large proportion of *cinnamic acid* and some *benzoic acid.* When it is decomposed with melted potash, parabenzoic and protocatechuic acids, pyrocatechin and resorcin are formed. In nitric acid the balsam dissolves readily, and yields abundance of picric acid, together with oxalic and nitrobenzoic acids.

The *xanthorrhœa* resins have long been used in Australia as a remedy for gastric troubles, intestinal catarrhs, diarrhœas, etc., and are occasionally prescribed in this country for similar conditions; but their principal uses are in the arts as a source of picric acid, and in the manufacture of lacs and varnishes.

Dose, from 0.5 to 1 gm. (gr. viij. ad xvi.). It may be given in alcoholic solution.

W. P. Bolles.

XANTHOXYLUM. See *Ash, Prickly.*

XERODERMA. See *Ichthyosis.*

XEROFORM. See *Tribromphenol bismuth.*

XEROSTOMIA. See *Parotid Gland, Diseases of.*

X-RAYS. See *Roentgen Rays, etc.*

XYLOL.—A hydrocarbon, or mixture of isomeric hydrocarbons of the composition $C_6H_4(CH_3)_2$, occurs as a constituent of coal-tar, and is known as *xylol* or *xylene.* This substance is principally *metaxylene* (*metadimethylbenzene*), with a certain proportion of *paraxylene* (*paradimethylbenzene*), and possibly some other hydrocarbons. Pure metaxylene can be obtained by special processes. Xylol is a thin, colorless fluid of a faint odor, reminding somewhat of that of benzene, and of a burning taste. It is insoluble in water, but soluble in alcohol. Medicinally, xylol has been used in the treatment of smallpox, and had at one time an ephemeral, but undeserved, reputation as a remedy for the disease. It was administered internally in doses of from ten to fifteen drops, in emulsion, and was also applied locally to the throat. It is now obsolete as a medicine.

Edward Curtis.

YADKIN MINERAL SPRINGS.—Stanley County, North Carolina.

Post-Office.—Palmersville. Boarding-houses.

Access.—Viâ Southern Railroad to New London, thence six miles by private conveyance to springs.

This resort is charmingly located in a wild and picturesque region penetrated by the Yadkin River, and covered by the Oconsechee Range of mountains. Like the usual North Carolina mountain climate, the atmospheric conditions prevailing in this section are eminently conducive to good health and longevity. The rainfall at the springs is about fifty-three inches annually, and is quite uniformly distributed through the seasons. There is no hotel, but during the season, from May to November, accommodations may be obtained at a reasonable rate in a number of private boarding-houses. The springs are two in number, a chalybeate spring yielding sixty gallons of water per hour, and a sulphur spring flowing at the rate of one hundred and eighty gallons per hour. No qualitative analysis is available. Much beautiful scenery is found in the neighborhood of the springs; the falls of the Yadkin River, the Narrows, and the "Devil's Den," a great cave in the hills, being the most prominent.

James K. Crook.

YARROW.—*Achillea, Milfoil. Achillea* L. (fam. *Compositæ*) is a genus of more than one hundred species, several of which, from ancient times, have been used in domestic and professional medicine. The most important of these is *A. millefolium* L., the herb of which is used. It is a perennial plant, indigenous to Asia and Europe and largely naturalized (or perhaps native) in North America. Its active principles are a very small amount of a volatile oil, and the bitter glucoside *achillein.* Aconitic acid also occurs, with considerable tannin, a little gum and resin. The drug is to be classed as an ordinary aromatic bitter, somewhat like chamomile. The dose varies from 0.3 to 2 gm. (gr. v. to xxx.).

Henry H. Rusby.

YAWNING.—(Synonyms: Gaping, Oscitation; Germ., *Gähnen;* Fr., *Bâillement.*)

Definition.—Yawning is a physiological modification of respiration by which the act is intensified. It consists in an involuntary, forcible, and profound inspiration, followed by a pause and a prolonged expiration. When fully developed, it is accompanied by a wide opening of the mouth, an elevation of the velum palati, and depression of the larynx, a roaring sound, and usually a click in each ear, a flow of saliva, and a suffusion of the eyes with tears, and a more or less imperative impulse to extend the limbs, especially the arms (pandiculation), to bow and twist the trunk, and to throw back the head. The inspiratory act is frequently audible, and the expiration usually acquires a distinct blowing sound. The elevation of the palate closes the posterior nares and causes the air to be admitted wholly through the mouth. In the same way the Eustachian tubes are closed, causing momentary obtunding of hearing. The contraction of the palatal muscles often precedes the opening of the mouth, and tends to persist for a moment after its closure. The commencement of their contraction is not infrequently accompanied by a rapid succession of three or four short, broken inspiratory efforts.

Physiology.—Yawning is a physiological expression of fatigue and a disposition to sleep. It may, however, arise from a retardation of the respiration, or from any influence which will impair the oxygenation of the blood. It is frequently, therefore, a product of melancholy, languor, ennui, torpor, or debility, or of the malaise which precedes the onset of disease. It is liable to follow prolonged abstraction of mind or concentration of thought. It is sometimes the result of feeble or laborious digestion,

of gastralgia, or of other disorder of the digestive organs, or it may occur in response to a demand for increased activity of circulation. It may be sympathetic. To some individuals it is habitual, occurring without fatigue, and being but the outgrowth of the lassitude or indolence of their natures. It may sometimes be attributed to the possession of an inferior degree of intelligence, a slothful, inactive, effeminate, timid, or lustful disposition incapable alike of vigorous mental exertion or of prolonged physical activity.

That yawning may be the response to a demand for increased activity of oxygenation in the lungs is demonstrated by placing an animal in an irrespirable atmosphere. Repeated yawning occurs shortly before the animal succumbs to asphyxia. The phenomenon is therefore usually explained on the supposition that it is due to a stimulus transmitted from the central nervous system in response to a peripheral impression, in most cases arising, in part at least, from the respiratory apparatus. Longet has attributed it to the accumulation of too great a quantity of venous blood in the right side of the heart, whence the peripheral impression is supposed to proceed. From whatever source we derive the peripheral impression, however, the act is generally admitted to be reflex in character. Of the reflex nature of the stimulus which produces the muscle contractions in the extremities, there can be no doubt; for it is a matter of repeated observation that the hand which, owing to paralysis, has been for years beyond control of the will, and has become firmly contracted by post-paralytic rigidity of its flexor muscles, will often become distended during yawning. It is evident here that the stimulus can emanate only from the spinal centres.

The mechanism of yawning is the same as that of normal respiration; the same muscles are called into action, but their movements are more extended. (See *Respiration*, Vol. VI.) The diaphragm, the scaleni, the sterno-cleido-mastoids, the clavicular portions of the trapezii, the lesser pectorals, the subclaviculars, the external intercostals, the serrati magni, the rhomboids—in fact, all the muscles which normally act as direct or as auxiliary forces in the full expansion of the chest, take part in the inspiratory movement; and all the muscles of forced expiration are called into action in the expiratory stage. In the fully developed yawn there is the action also of the muscles of the face, the depressors of the lower jaw, the dilators of the nostrils and upper lip, the orbiculares palpebrarum, the zygomatics, and of the depressors of the hyoid bone and larynx, and finally of the muscles of the back in the bowing of the trunk, and of the extensors of the extremities when stretching occurs.

Yawning is involuntary. It begins without the sanction of the will, and, once begun, it cannot be arrested. In this it resembles sighing, sneezing, hiccough, and other modifications of respiration, without, however, possessing their full spasmodic quality. Yet the will is not entirely deprived of influence over it; for a yawn may be often in a measure concealed by a forcible effort at closure of the jaws, and the mouth may be closed before the yawn has subsided. It may be imitated, but no amount of effort will induce it unless a sufficient cause for it exist. As Carpenter says, "this act may be performed by the will, though not completely; and is one that is particularly excited by an involuntary tendency to imitation, as every one must have experienced who has ever been in company with a set of yawners."

After yawning there is usually a momentary pause in the respiratory movements, followed by normal, tranquil breathing. The forced respiration has not only supplied the blood with its needed oxygen, but, aided by the muscular contractions, has removed venous engorgement and accelerated the systemic circulation. At the same time, a moment's relaxation has been given to the fatigued body, and a sense of relief is usually afforded.

Symptomatology.—The value of yawning as a symptom has been at different times very differently estimated. Hippocrates recognized it as a precursor of a fever, particularly of intermittent fever. From its frequency and intensity he prognosticated the severity and duration of the disease. Yawning, with suffusion of the eyes and pandiculation, was in early times among the most valued factors in the diagnosis of the eruptive fevers. Occurring during parturition, it was an evil omen. Roederer, in 1759, believed that he had observed a death from it. The yawning of the infant was also a cause for solicitude.

It is now comparatively seldom, however, that we think of yawning as more than an indication of fatigue and a precursor of sleep, or of lassitude and a lazy disposition. But that it may denote a diseased state of the system is a well-recognized fact. As indicative of fatigue, it may be a symptom of profound mental or physical exhaustion. It may, in fact, of itself constitute a morbid condition of spasmodic nature and of grave import. It is not infrequently indicative of a deficient oxygenation of the blood, especially when it is associated with the dyspnœa which results from the lung consolidation of fibrinous pneumonia, the lung compression of hydrothorax or pneumothorax, or after profuse and exhausting hemorrhages. In the latter connection, it is at times a valuable factor in the diagnosis of concealed hemorrhage.

Modern experience has but confirmed the observations of the ancients with regard to the occurrence of yawning in the prodromal stage of fevers, particularly of the intermittents. In these, as also in such neurotic affections as epilepsy, hysteria, catalepsy, and somnambulism, frequent gaping often signifies the immediate supervention of a seizure. When it occurs during the course of a disease it not seldom indicates the approach of resolution or of a crisis. It is so frequently observed during parturition, however, as a consequence merely of fatigue, that no great significance is now attached to it.

As a symptom of feeble or suppressed menstruation in anæmic young girls, it is probably in most instances a manifestation of hysteria, so often a complication of this disorder. It is probable also that many of the reported cases of spasmodic yawning have been of hysterical origin. Nevertheless, cases have been reported in which yawning of a spasmodic character developed without hysteria, and resembled whooping-cough, spasmodic laughing, crying, sneezing, etc. Of a reflex nature, the affection may be indicative of various disorders of the central nervous system, particularly of cerebral anæmia, of circulatory disturbances in the medulla oblongata, or it may occur in the wake of cerebral hemorrhage. It also shows a predilection for individuals who, from necessity, are confined to small, closely crowded work-rooms, and for convalescents from neuralgic affections, especially cardialgia and hemicrania.

To the surgeon yawning is of interest chiefly on account of its occasionally producing luxation of the lower jaw. The mechanism of this accident is considered under *Dislocations*, in Vol. III. *James M. French.*

YAWS is a chronic, highly contagious disease, probably caused by a micro-organism, confined to certain tropical countries, and characterized by a peculiar cutaneous eruption which goes through the stages of squamæ, papules, and tubercles; it is accompanied by a variable (but generally slight) amount of constitutional disturbance, and tends to recovery.

Synonyms.—Yaws is the common name given to this disease in the British colonies and by the negroes from West Africa. Sauvages, in 1759, suggested *frambæsia* as the scientific name, from the resemblance of the split tubercle to a raspberry (*framboise*); though Rat thinks that the characteristic tubercle is more like the top of a pickled cauliflower than a raspberry. Charlouis, in 1881, proposed *polypapilloma tropicum;* and later, Nicholls has suggested *granuloma tropicum* as a more correct and scientific designation. And it is to be regretted that one or other of these two names has not found universal acceptance. Different places, too, have furnished different names for this disease, the chief of which are as follows: In the French West Indies it is called *pian;* in Brazil and the Spanish and Portuguese possessions, *bubas,*

bobas; in Ceylon, *parangi*; in the Dutch Indies, *patek*; on the Gold Coast, *ajortor*, *dube*, *dabai*, *tongara*; in Calabar, *framosi*; in Congo, *tata*; in Samoa, *lupani*, *tomo*; in Fiji, *coko*; in New Caledonia, *tonga*, *tono*; in the Moluccas, *bouton d'Amboine*.

Geographical Distribution.—Yaws is endemic in the tropics, chiefly in the West India Islands (notably Dominica and Jamaica), Central and South America, Western Africa, Mozambique, Madagascar, Ceylon, Java, the East Indian Archipelago, and Polynesia. Its limits seem to be ten degrees on each side of the Equator; though lately cases have been reported from Kimberley, in South Africa. Negro slaves from Africa probably took the disease to the West Indies. The first account of the affection was given by Oviedo in 1525; he met with it in Hispaniola (now St. Domingo).

Etiology.—The direct cause of the disease is undoubtedly a micro-organism, but so far it has not been absolutely identified. Hirsch, Pierez, and Nicholls and Watts have reported the finding of a micrococcus, to which they ascribe the disease; Breda attributes yaws to a bacillus; and Powell to a yeast. Yaws is generally acquired by direct contagion, and is inoculable through a sore, or an abrasion of the skin, also by the nipples of a nursing mother or the mouth of an infant; but flies, mosquitoes, and other insects may also be the means of disseminating the disease. It is also transmitted by clothes, rugs and mats, and dirt from the floor or walls of filthy and infected hovels. As predisposing factors may be mentioned: *Age*. Infants below one or two years are generally exempt; children between two and fourteen years are most liable to be attacked by the disease. *Sex* has but little influence, the number of males affected being slightly in excess of the females. *Race*. The negro is much more liable to yaws than the white man or mulatto. *Hygiene* is an important factor in this apparent immunity of the whites; and the negro's absolute ignorance of and indifference to things hygienic will go far to explain his susceptibility to yaws. A constitution worn out by disease or dissipation and unhygienic surroundings are potent predisposing factors. *Heredity* plays no part, for children are not born with yaws; this is an important difference between this disease and syphilis. But Hallen has reported a case of yaws in an infant twenty days old. The mother was suffering from yaws and the child probably got infected during labor. *Vaccination* seems to have a favorable influence on the disease. In persons who have been vaccinated an attack of yaws is generally very mild, while a similar result is often experienced from vaccinating a person suffering from yaws. One attack of yaws usually confers *immunity* from future attacks, at any rate for a number of years; but occasionally a person acquires the disease a second or even a third time.

Symptoms and Course of the Disease.—The disease begins with a *period of incubation*, of from two to eight weeks (but generally nearer the former figure), and lasting till the appearance of the local lesion. Usually there are no prodromes, and occasionally there are a few vague symptoms, such as malaise, languor, headache, itching, pains in the limbs, vertigo, constipation, fever, and palpitation of the heart. In children these symptoms are apt to be more pronounced. This is followed by *the eruptive stage*, which may last for a period varying from a couple of months to as many years. The symptoms mentioned above become more pronounced, and the skin becomes dry, scaly, and lustreless, and in the negro lighter in color. This squamous eruption soon gives place to papules, one or more of which may sometimes be found, on close examination, at the seat of the inoculation. These papules at the point of inoculation may either heal (with treatment in about two weeks, or without treatment in about two months), or break down and ulcerate. They are most apt to appear on the face, perineum, areola of the breast, genitals, anus, toes, lips, mouth, and nose; also at the junction of the mucous membranes with the skin. The papule, which at first is about the size of a pinhead, grows to the dimensions of a pea or a pingpong ball, or even larger. It is conical in shape, and the skin over it becomes thinner and redder and more shiny, and eventually splits in the centre of the tubercle or granuloma, as it is now called. On the splitting of the skin there appears a raw protuberance which seems to push itself through the epidermis; this is the "*framboise*," and is often covered with an offensive exudate of a dull seropurulent fluid, which forms a scab; and this, if removed, is replaced by new crusts. The surface under these crusts is red except in cachectic individuals, when it is of a dirty-yellow color. These tubercles are either single or they coalesce, or they may appear in successive crops; they are the essential lesion of yaws. They may measure as much as two or three inches in diameter, and a quarter of an inch in thickness. They are not painful or tender to pressure, except when they are situated in the palms of the hands or the soles of the feet or under the nails. When situated in the axilla or on the thigh they are apt, from pressure, to become flat. The tubercles gradually shrink, and the scabs or crusts drop off, leaving only a macule which itself eventually disappears. The lymphatic glands in the immediate neighborhood are sometimes involved, in which case they become swollen, and may even suppurate. During this stage some squamæ and papules may also be present. A few papules occasionally remain after the others have disappeared, and are called by the negroes "*memba*" *yaws* ("*memba*" being equivalent to *remember*). In a mild case of yaws there are no sequelæ; but in severe cases and in the debilitated and dissipated there may be serious ulceration, also bone lesions; but the latter are more apt to be a result of syphilis, and the possibility of this disease being present with yaws must not be overlooked. At the same time care must be taken not to give too much mercury, or serious results may follow, for which the yaws is not responsible.

Irregular Varieties.—Occasionally one of the yaws tubercles is larger than the others, is more or less isolated, comes earlier, or lasts longer, and is considered by the negroes to be responsible for the other tubercles; such a one is called a "*maman*" *pian* or "*mother*" *yaw*. When the soles of the feet and palms of the hands are affected, there is apt to be severe inflammation; and the disease thus localized is called *crab yaws*, *crabs*, *crappox*, *tubboes*, or *tubba*. *Ringworm yaws* is the name given when the papules become confluent and are arranged circularly.

Pian d'artre is the name given when most or all of the tubercles are replaced by yellowish spots slightly elevated.

When a number of tiny vesicles remain scattered over the trunk the condition is called *Pian gratelle*. This is an occasional sequel of yaws.

Diagnosis.—The transition of the squamæ to papules and later to tubercles which split and exhibit a tumor with a yellowish discharge, is fairly characteristic of yaws. Syphilis is the disease with which yaws is most likely to be confounded. Hutchinson believes yaws to be a species of syphilis modified perhaps by climate and race, but still syphilis. Pierez, Powell, Nicholls, Rat, and most other observers believe that these two diseases are absolutely distinct. Among the points of difference may be mentioned: 1. Yaws is practically confined to the tropics, while syphilis is found almost everywhere. 2. Yaws is not hereditary; syphilis is hereditary. 3. In yaws the primary lesion when found is a soft ulcer; in syphilis it is a hard chancre. 4. Yaws does not invade the nervous system or viscera; syphilis attacks both. 5. In yaws there is considerable itching; in syphilis none. 6. The eruption in yaws is characteristic and *sui generis*; that of syphilis is polymorphous. These are enough to differentiate between the two diseases; but it must be remembered that both syphilis and yaws can occur in the same patient.

Pathology.—According to Macleod ("Pathology of the Skin"), the clinical lesions, namely, squames, papules, and tubercles, are stages in the evolution of a common histological process.

I. "*Changes in the Corium.*—1. Blood-vessels: Dilata-

tion, and tortuosity of those in the papillary and subpapillary layers; no thickening of the vessel walls or endothelial proliferation; vessels persist in the granuloma. 2. Cellular infiltrate consists of: (*a*) Plasma cell infiltration at first most marked in the neighborhood of the vessels, follicles, and glands, rapidly becoming diffused; no definite arrangement in rows; no large multinuclear cells or true giant cells. (*b*) Mast cells, connective-tissue cells, and small mononuclear cells; no tendency to organization detected. (*c*) Marked extravasation of polynuclear leucocytes. 3. Fibrous stroma: (*a*) Collagen attenuated where the granuloma is densest; no definite degeneration. (*b*) Elastin similarly affected. 4. Hair follicles, sebaceous glands, and coil glands seemed healthy.

"II. *Changes in the Epidermis.*—1. Marked proliferation and down growth of the interpapillary processes so great in the older lesions as to resemble condyloma acuminatum. 2. Basal layer interrupted. 3. Œdema affecting prickle cells and interepithelial spaces. 4. Disappearance of pigment in the affected area. 5. Transitional layers imperfect. 6. Cornification; marked hyperkeratosis and parakeratosis, with deposition of leucocytes and débris between the horny lamellæ." (Macleod.)

Prognosis.—This is favorable, as the disease nearly always terminates in recovery. Under proper treatment a period of a few months suffices for restoration to health. Very young children and the feeble and dissipated may die of exhaustion.

Treatment.—Cleanliness and proper hygiene are the best prophylactic measures. The first step in treatment is the segregation of those afflicted. So necessary has this been found that in some of the West India islands, *e.g.*, Dominica, there are yaws hospitals to which those suffering from the disease must go under penalty of imprisonment. Actual treatment consists in cleansing the patient, then in the use of local antiseptic washes, good nourishing food, and tonics. The drugs most often used are: iron, arsenic, iodide of potassium, mercury. The bowels must be regulated, and any concurrent diseases, such as syphilis, be appropriately treated. In *crab yaws* the feet and hands should be soaked in hot water and the softened skin then pared away till the yaw growth is exposed; it can then be treated as mentioned above.

R. J. E. Scott

Literature.

Scheube's Diseases of Warm Climates; Hirsch's Geographical and Historical Pathology; a paper by Pierez, in the Transactions of the Pan-American Medical Congress of 1893; an article by Firth in Allbutt's System of Medicine; and an article by Nicholls in the Twentieth Century Practice of Medicine; with the bibliography supplied in each.

YEAST.—(*Cerevisiæ Fermentum; Leaven.*) The fungus *Saccharomyces Cerevisiæ* Meyer (tam *Saccharomycetes*), in its commercial forms more or less mixed with vegetable substances constituting its nutrient medium.

The alcohol ferment so well known under the name brewers' yeast, consists chiefly of living cells of the plant named above, mixed according to convenience with starch, sugar, malt, meal, or similar substances, and sometimes with hops.

This little plant consists, in its usual form, of single ovoid cells containing turbid protoplasm and vacuoles (*vide* Fig. 5045, *i*) about the $\frac{1}{2000}$ of an inch in length. These cells, in active yeast, increase in numbers to an incredible extent by budding (Fig. 5045, *ii*, *iii*, *iv*), usually separating almost as fast as the new cells attain any considerable size, but also often, especially upon the surface or where the fermentation is slower, cohering for a while in colonies (*v*); under rare circumstances, mother cells (asci ?) are formed in which two or several cells are differentiated, and finally liberated by the disappearance of the original cell wall; these then grow and bud in the same way as the preceding. During the growth and multiplication of these little cells starch and the different sugars are ultimately disintegrated into alcohol and carbon dioxide. (See the articles on *Bacteria*, *Enzymes*, and *Fermentation*.)

The early history of yeast is lost in antiquity. It is frequently mentioned in the Bible as leaven, and in some shape or another has been, and is, used by nearly all races of mankind; its production in the great beer and spirit breweries of Europe and America amounts to thousands of tons, and it is consumed and often made in nearly every family of Christendom.

As a commercial product, yeast exists in three principal forms: (1) Brewers' yeast (formerly official in England), the skimmings of the fermenting beer vats, containing the plant in a state of high activity, of which the following

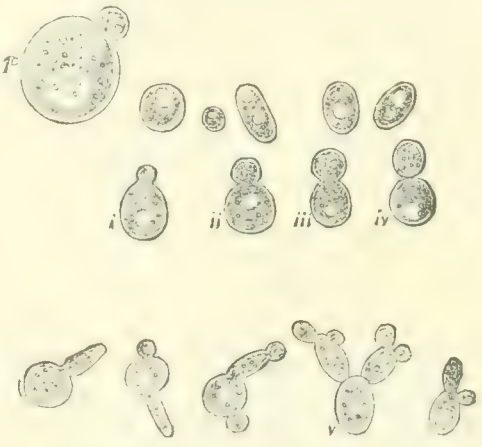

Fig. 5045.—Cells of Ordinary Brewer's Yeast. (Copied from an Atlas of Practical Elementary Biology, by G. B. Howes, London, 1885.) *i*, *ii*, *iii*, *iv*, Stages in division of the same cell; *v*, cell *i* as seen under Gundlach's one-sixteenth immersion lens; *v*, a branching colony, the cells of which still retain their original connections.

was the official description: "Viscid, semi-fluid, frothy, exhibiting under the microscope numerous isolated, roundish, or oval cells, or short-branched filaments composed of united cells; odor peculiar, taste bitter"; (2) cake yeast (dry) consists of the above mixed with starch flour or, usually, in this country, Indian meal, rolled and cut into little biscuits and dried; and finally, (3) superseding both the above forms for domestic use in cities and towns, the German or compressed yeast in little moist cakes enclosed in tinfoil, which consists of an almost solid mass of yeast cells with a minimum of starch or sugar. This is made by taking the beer skimmings and repeatedly washing and straining them, and allowing the cells to settle, and finally pressing nearly dry between cloths; or by propagating them in a definite mixture of barley-malt, rye flour, and barley, and collecting, washing, and pressing in the same way. "Compressed" yeast is a very concentrated and active form of yeast. In its moist state, however, it does not keep very well, and should be obtained fresh every day or two, and laid in the ice chest until wanted.

Whether the characteristic properties of yeast are dependent upon the existence and manifestation of life in the plant, or are merely the result of chemical activity on the part of some principle capable of extraction in an active state, has been an intensely interesting and highly important question ever since the discovery of active constituents in plants. The most recent experiments by Büchner seem to prove that the latter is true, the enzyme *zymase* having been described by him. Since it is incapable of escaping through the pores of the cell wall, its extraction is dependent upon a process of extreme disintegration. Zymase retains its properties after extraction for only a comparatively short period, a few months being the longest time recorded.

Into the general uses of yeast it is not the design of this article to enter. It is concerned in the production of all beers, wines, and liquors, and of the common "raised" breads and cakes. As a modifier of food in these instances it has considerable dietetic importance; when

mixed with a moderately thick dough, the disengagement of carbonic acid taking place throughout, fills it with innumerable minute interstitial bubbles, or makes it spongy, as the housewives say, or light. If baked in this condition these bubbles expand with the heat, making the bread still "lighter," or more porous, and in a condition for more ready disintegration in the stomach and intestine than breads made without yeast, and depending upon the vaporization of water only for their lightness. The alcohol is mostly dissipated in the baking and cooling of the bread; the cooked yeast itself is probably of no special dietetic consequence.

In medicine yeast is now scarcely used. It has been given in indigestion, dyspepsia, etc., but is of little consequence (there are yeast cells in or upon our food almost always). Dose of liquid yeast, 15 or 20 gm. (ʒ ss.). It still survives to a moderate extent as a poultice (*Cataplasma Fermenti*), which is simply a thin raised dough.

Take of beer yeast, 6 fluidounces; wheaten flour, 14 ounces; water heated to 100° F. (37.8° C.), 6 fluidounces. Mix the yeast with the water and stir in the flour. Place the mass near the fire till it rises.

Yeast poultice is a light, agreeable application, and is thought to overcome the odor and reduce the decomposition of sloughing sores. It is seldom used in this country.

W. P. Bolles,
Revised by *Henry H. Rusby.*

YELLOW FEVER: HISTORICAL SKETCH OF THE DISEASE, ITS ETIOLOGY AND MODE OF PROPAGATION.—History.—The remotest records about epidemic diseases in the Old World fail to show that yellow fever or any other disease presenting similar epidemiological features had ever been observed previous to the discovery of America in 1492; while in the newly discovered lands it soon became apparent that every expedition of European settlers that came to the Antilles or to the Spanish Main had to pay a heavy tribute to an unknown pestilence, during the first summers of their residence, suffering thereafter no further trouble from the climate. Was this pestilence yellow fever?

In order to answer that question Bérenger-Féraud and I, independently of each other, undertook minute historical researches, some fifteen years ago. We both came to the same conclusion: that the disease mentioned in the old Spanish chroniclers as the "peste," "contagio," or "epidemia," was no other than our modern yellow fever; and that, at the time of the discovery, it was endemic on the coast of Mexico, at the present site of Vera Cruz, as well as on the Atlantic side of the isthmus, and on the Spanish Main along the coast of Colombia and Venezuela inhabited by the Carib Indians. These warlike Indians were constantly plying across the Caribbean Sea in their canoes, and through them yellow fever appears to have been sometimes conveyed to their own Isles of Dominica, Guadeloupe, Porto Rico, and to the eastern end of Hispaniola (the Province of Higuey in Santo Domingo) which was often visited, if not held in actual subjection by that fierce Indian tribe. The disease was called "Poulicantina" by the Caribs (Bérenger-Féraud) and "Cocolitzle" by the Mexicans (see my "Epidemiologia primitiva," in Cronica Medico-Quirurgica de la Habana, Mayo 15, 1897).

The Caribs maintained in captivity upon their own isles a number of women and youths captured by them from the peaceful and even timorous tribes who dwelt upon the greater Antilles, the male adult prisoners having been disposed of to satisfy the cannibal instincts of the captors. Being born or bred in the endemic foci on the mainland, the Caribs must have been immune against the Poulicantina, just as the natives of Cuba have been hitherto against yellow fever; but the presence of the non-immune captives may have supplied the required material for the occasional development of poulicantina epidemics in the Carib Isles, and also in the Higuey district of San Domingo; and in this way the disease could readily have reached any foreigners who chanced to visit those islands. This is indeed what seems to have happened to the Spaniards, newly arrived in Hispaniola, during a long succession of summers ever since their first settlement in 1494; and to the French ever since their first attempts to colonize the Carib Isles, one and a half centuries later. The French missionaries, less reticent than the Spanish colonists had been, made no mystery of the symptoms of the epidemic disease which attacked them, and which, they said, was known in the Spanish Islands under the names of "peste" or "epidemia"; so that the identity between our modern yellow fever and the poulicantina as well as with the "peste," "contagio," "epidemia," of the Spanish colonies, could no longer be doubted, after the description of Du Tertre, who witnessed the epidemic of Guadeloupe in 1648, and Cogolludo's minute account of that of Yucatan the same year.

First Names Given by the Spaniards to the Pestilential Disease which Attacked the Spanish Settlers Newly Arrived in Hispaniola and Darien.—On the 2d of February of 1494, two months after the arrival of Columbus at Hispaniola, on his second voyage, bringing with him the first European expedition (fifteen hundred men) that ever set foot on American soil, twelve of the seventeen vessels on which that expedition had come sailed away, under command of Antonio Torres, for Spain, taking, no doubt, the route through the Canary Islands which was still followed in those days. At the port of departure where the colonists, by order of the admiral, were building the town of Ysabela, most of the men had been falling sick since the last week of January; but though many were on the sick list only few died. Critics are mostly agreed in attributing to malarial fevers the illness which attacked the men at this time, the admiral himself having been one of the sufferers. It is possible, however, that some of the fatal cases may have been yellow fever. At any rate, as the year advanced, the situation became more critical, and by the end of May, when the admiral's brother, Bartolomé Colon, arrived with three vessels laden with provisions from Spain, sickness and death had been rife among the Spanish settlers in Hispaniola, not only at the port of Ysabela, but also in the interior of the island where forts had been constructed near the gold mines. The Indians then began to run away from their masters, deserting the culture lands, perhaps in order to preserve themselves from a contagion with which they were already familiar; but the Spaniards attributed their dispersion to a preconcerted plan for starving the foreign invaders out of their country by not planting at the proper season the vegetables upon which the inhabitants were most dependent for their subsistence. Oviedo attributes to this action of the Indians the great mortality which followed. From two-thirds to one-half of the Spaniards died, but innumerable were also the deaths among the Indians themselves, whose cadavers lay strewn in the fields, producing, says the chronicler, a most horrible and pestilential stench. Columbus, in the mean time, had been absent from the island since the end of April, exploring the coasts of Cuba and Jamaica, and intending also to visit Porto Rico. About the middle of September, on his way from Jamaica to Porto Rico, he came close to the shore on the south coast of Hispaniola, holding intercourse with the Indians and landing nine men of his crew to convey information about his own movements to his people at Ysabela, across the island. He was detained by a severe hurricane during seven or eight days in a narrow pass between the coast and the islet of Saona, close to the Higuey district. On the 25th or 26th of September, as he was proceeding toward Porto Rico, he was suddenly attacked by a grave illness, which deprived him of his senses and so much alarmed the crew that they turned from their intended course and brought the admiral and the other two vessels back to Ysabela, where they arrived on the 29th. He continued several days ill, and had a long convalescence, probably prolonged by a return of his malaria infection, as often happens in Cuba in the convalescence of yellow fever. In a letter which the admiral wrote to the King, he states that his illness on that occasion had been a "modorra pestilencial," prob-

ably the name which Dr. Chancas, the physician attached to the expedition, had given to the disease which had been causing so many deaths on the island since the admiral's departure in April. This same pestilential disease appears also to have been carried from Hispaniola to the Canary Islands, either by the vessels of Antonio Torres, or, more probably, by the three which returned to Spain after having landed D. Bartolomé Colon at Ysabela; for Humboldt and Bonpland inform us that "what remained of the Guanches on the Island of Teneriffe perished mostly in 1494, in the terrible epidemic called the "Modorra." Though every subsequent expedition which landed at Hispaniola lost one-third or more of their contingent from the same pestilence during the first summers of their residence on that island, the chroniclers, warned by the panic which had been created in Spain by rumors of the first epidemic, were silent as to the name and symptoms of the disease, always attributing the great mortality to the bad quality of the food and to the change of climate. But in 1514, when Pedrarias Davila landed at Darien with a splendid expedition, among whom were the Chronicler Oviedo and Andagoya, both of whom had lived in former years in Hispaniola, a terrible epidemic broke out among the newcomers, causing seven hundred deaths in one month, and each of the above-mentioned authors declares that the cause of it was the "modorra sickness"; adding that after the newcomers had gone through that ordeal, the climate proved as salubrious to them as that of Spain. The name of "modorra" was, however, soon abandoned, probably because the stupor or coma which characterizes some particular epidemics of yellow fever (see Cornillac, ed. 1875; p. 423) was found to be a less constant symptom than Dr. Chancas had imagined. In subsequent years the uncompromising terms of "peste," "pestilencia," "epidemia," "contagio," were substituted, and continued in use till the end of the seventeenth century.

The names of vomito negro and yellow fever were first given to the disease in the early part of the eighteenth century. In 1753, a surgeon of the Spanish navy, Dr. Josef Gastelbuondo, who had settled in private practice at Cartagena de Indias, published a book on the "vomito negro," stating in his preface that he had been studying the disease and investigating its causes during the previous forty years, and had performed several autopsies. Strange to say, he attributes the disease to the same causes which had been constantly invoked by the early Spanish colonists of the two previous centuries, namely, to the change of climate and to the poor quality of food for which the newcomers were unprepared. Other names such as typhus amaril, typhus ictérode, hæmogastric pestilence, malignant remittent, putrid fever, etc., continued, however, to be used conjointly with that of "vomito negro," yellow fever, fièvre jaune, febre gialla, till the commencement of the nineteenth century.

During the first two hundred years after the discovery of America the ports of Santo Domingo, Cartagena de Indias, Porto Bello, Darien, Vera Cruz, where the "flotas de Indias" brought each year, during the summer months, a large number of non-immunes from Spain, yellow fever assumed the character of a permanent endemic, while on the Island of Cuba, owing perhaps to its cooler climate and to the fact that its communication with Spain was less direct, the disease obtained a permanent foothold only in 1761, after the occupation of Havana by the English and the subsequent opening of Cuban ports to general commerce. Since that time and until 1901 Havana has been considered a constant menace of yellow-fever infection for the United States and for European ports. Rio de Janeiro, Brazil, on the other hand, has become an endemic focus only since 1850.

New Orleans also was at one time considered an endemic focus of yellow fever, not less than forty-eight epidemics having been recorded in the first sixty years of the nineteenth century; but the success which has followed the observance of strict quarantine measures after the civil war plainly shows that the infection of that port had in reality been derived from repeated importations from Vera Cruz, Havana, Central America, or from the West Indies. The propensity of yellow fever to spread into neighboring countries, along the lines of traffic, and to be carried in ships to far distant ones when certain climatic and topographical conditions are realized, has been verified again and again, causing innumerable victims as well as serious financial distress, and spreading terror over large areas in North and South America, on the western coast of Africa, in the Canary Islands, in the southwest part of Europe, and at times reaching as far north as Quebec and Swansea, and as far south as Montevideo and Buenos Aires. The climatic and topographical conditions to which reference has been made are essentially those which are compatible with the existence and functional activity of the insect which, as will be seen, assumes the rôle of a natural transmitter of the yellow-fever infection; the principal ones being the prevalence of temperatures between 70° and 90° F, low levels above the seaboard, proximity to the sea or to watercourses, and protection from strong winds. There is, however, another condition which must be inferred by reason of the geographical distribution of the disease, but for which no satisfactory explanation has yet been offered. I refer to the fact that while yellow fever is so frequently carried over the waters of the Atlantic Ocean, and, very exceptionally, far into the Mediterranean Sea, it is a remarkable fact that there is no record of the disease having ever been conveyed over the waters of the Pacific Ocean beyond the western coast of America, where epidemics have often occurred. Whether or not this fortunate state of things will continue after the Panama canal is thrown open, must be a matter of conjecture; but the bare possibility that it might not so continue should be borne in mind and act as a stimulus for all nations interested in the matter to urge the stamping out of yellow fever from the Caribbean Sea and the Gulf of Mexico, as well as from the western shores of America, before free communication is established between the waters of the two oceans in the very heart of the yellow-fever territory *par excellence*.

For a detailed account of yellow-fever epidemics in different countries the readers must be referred to Bérenger-Féraud's valuable chronology of the disease ("La Fièvre Jaune," Paris, 1890), and to Dr. G. M. Sternberg's article in the first edition of this HANDBOOK.

ETIOLOGY AND MODE OF PROPAGATION.—In the first edition of this HANDBOOK, Dr. G. M. Sternberg expressed himself in the following terms regarding the etiology of yellow fever.

"As to the nature of the *specific cause* of the disease there can scarcely be two opinions. The present state of science justifies the belief that it is a living micro-organism, and facts relating to the origin and extension of epidemics show that, as in cholera and in typhoid fever, this micro-organism is capable of development outside of the human body under conditions which will be discussed hereafter. Unfortunately, the present state of science does not enable us to give an account of the deadly microbe which we assume to be the cause of the disease under consideration. We know to-day the morphological and physiological characters and the habitat, within the body of an infected individual, of the specific cause of cholera, of typhoid, and of relapsing fever, but the researches made up to the present time have failed to demonstrate the 'germ' of yellow fever" (REFERENCE HANDBOOK OF MEDICAL SCIENCES, Vol. VI., 1887).

My tetragenus febris flavæ (M. tetragenus versatilis Sternberg) fared no better under Dr. Sternberg's keen criticism than did the *germs* of Freire, Carmona, or Gibier, nor shall I at present renew my claim as to its etiological significance; but I think it worth while recording the following remarkable coincidence. In 1895, in a paper on "Tetracoccus Versatilis," which was published in the *Edinburgh Medical Journal* (December, 1895), I called attention to the curious circumstance that pure cultures of my tetragenus, which had been filtered through Kitasato filters, had on two occasions given evidence that some of the tetragenus germs had passed

through the pores of the filter; while in 1901, in the last experiments performed by the United States Army Board, we are informed that the blood serum of a yellow fever patient, after being passed through a Berkefeld filter, gave evidence that the germ had passed through the filter, for positive results were obtained when the filtrate was injected into non immunes, and Drs. Reed and Carroll infer that the said germ must be ultra-microscopic (see the article published by Drs. Reed and Carroll in *American Medicine*, February 22d, 1902, p. 304). Should the fact be confirmed that my tetragenus possesses ultra-microscopic spores besides the coarser forms which it develops in our artificial culture media, most of the objections which have been raised against its etiological significance would fall to the ground.

In 1897 Dr. Sanarelli discovered in his cultures from yellow-fever material collected in Brazil a new bacillus which he still considers the specific germ of the disease. This discovery attracted a good deal of attention, having been confirmed by some other observers, while others again strenuously denied that it had any etiological significance. The unquestionable competence of the discoverer and his previous good record at the Institut Pasteur added considerable weight to his claim. A final verdict, however, was given against him after it was averred that his bacillus icteroides never developed in any of the bouillon tubes that were planted, by Drs. Reed, Carroll, and Agramonte, with samples of yellow-fever blood which, inoculated into non-immunes, invariably reproduced the disease. I believe, however, that the bacillus of Sanarelli may be one of the promoters of the secondary infections which characterize the hæmogastric forms of yellow fever, and in that capacity it may yet be found to constitute an important factor in the development of the worst complications which are apt to occur in the course of an attack of yellow fever.

However much it may be regretted, that up to the present day the specific germ of yellow fever has not been identified, so that the diagnosis of some abortive or atypical cases must often be considered problematic, it is, however, a great source of satisfaction that we positively know the manner in which the disease is transmitted in nature, and that this knowledge enables us to control with great success its propagation and to stamp it out, as has been done in Havana during the last sixteen months.

Discovery of the Yellow-fever Mosquito.—Apart from the historic interest which the matter might afford, I think it proper to acquaint the reader with the arguments which led to the discovery of the particular mosquito by which yellow fever is transmitted, inasmuch as, considered from an *a priori* point of view, those same arguments should prove more convincing than when they are presented merely as a sequel to the demonstration.

In 1880, after receiving the valuable report given out by Prof. Stanford Chaillé as president of the Havana Yellow-fever Commission of 1879, I undertook a careful revisal of all the facts which had been collected since 1853 in the United States, and arrived at certain conclusions which are here summarized in the form of propositions, and which afforded a solid foundation for my future investigations.

Proposition A. Though yellow fever must be considered to be a germ disease, it is transmissible only under certain topographical and climatological conditions which are realized at all seasons of the year only in certain localities along the Atlantic shores of tropical America, where the disease is considered endemic, and of which Havana might be considered a type.

Proposition B. Even within the infected foci, the disease is apparently not contracted through contact with the patient or his secretions, nor by breathing the air of the sick-room, nor by the use of contaminated food or drinks.

Proposition C. The pathological lesions pointed out by Crevaux, Gama Lobo, and other competent observers, in the walls of the blood capillaries of yellow-fever cadavers, and the hemorrhagic tendency which, as a rule, develops in the course of the attack, even in mild cases, suggested the idea that the mesoblastic tissue from which the vascular endothelium is formed might prove to be the most appropriate source from which the infective material could be obtained.

From proposition A, I had inferred that, for the production of a case of yellow fever, a third factor was required besides the yellow fever patient and a person susceptible to the infection—a factor which, though indispensable for the transmission, might exist independently of the patient and of the disease. It should, however, be essentially dependent for its existence and for its functional activity on the topographical and climatological conditions which favor the transmissibility of yellow fever.

From proposition B, I inferred that the only unexplored channel by which the virus or germ might prove pathogenic for human beings must be by a process of inoculation.

From proposition C, I surmised that in order that the inoculation should prove effective, the infectious material might be obtainable only from the blood or from the walls of the blood capillaries of a yellow-fever patient, and might require also to be inserted into the capillaries of a non immune.

I was thus led to conclude that the transmission was effected through the agency of some blood-sucking insect which was peculiar to yellow-fever countries, and which was able to retain upon its mouth parts the living germ so as to inoculate it afterward into those whom it chanced to bite. In searching for such an insect I came across the day mosquito of Havana (culex mosquito Desv., Stegomyia fasciata Theo.), in which I had observed certain peculiarities in the manner of laying its ova, and in its readiness to renew its bites whenever the digestion of a previous meal of blood had been completed, both of which peculiarities seemed to differentiate it from other species of gnats and to make it particularly well suited for the purpose of reproducing a disease in an epidemic form. Upon investigation I found that this insect was benumbed and unable to bite under the influence of temperatures of 15° C. (59° F.), at which degree of cold epidemics of yellow fever were known to cease in New Orleans, in Rio Janeiro, and in Havana; and also that after being kept for a while in a rarefied atmosphere corresponding to altitudes of four thousand to six thousand feet, at which elevation yellow fever is intransmissible, the insect lost to a great extent the power of driving its sting into the flesh.

My next step was to submit my theory to an experimental test by applying to non-immunes mosquitoes of that species which had been made to bite, two or three days before, a severe case of yellow fever. Among twenty non-immune soldiers who were set apart and kept under observation during two months, five were on different dates bitten by a mosquito which had been contaminated in that manner. Three of the five were taken sick after their inoculation, one after fourteen days with a mild but characteristic attack of albuminuric yellow fever, two were attacked on the fifth day after the inoculation with an abortive form of yellow fever, while neither of the other two showed any symptoms characteristic of the disease. None of the fifteen who had not been inoculated suffered any similar attack of fever during the two months that they remained under observation. After the lapse of four years I ascertained that none of my five inoculated soldiers had been reported again as suffering from yellow fever.

During the next twenty years I continued to perform that mild form of inoculation, my object being to ascertain whether or not some degree of immunity might thereby be obtained even when no immediate pathogenic effect had followed the inoculation. The principal data concerning each of the mosquito inoculations that were performed either by me or by my collaborator, Dr. Claudio Delgado, have been set down in Table 1., so that the reader may judge for himself and draw his own conclusions. Two of the inoculations (No. 3 and No. 104 of

Tables of Mosquito Inoculations Performed in Havana.

Abbreviations which are used in these tables:

"eph." ..... Ephemeral fever without characteristic symptoms.
"Abort." ..... Abortive yellow fever, with albuminuria.
"abort." ..... The same without albuminuria.
"N-a." ..... Non-albuminuric yellow fever with well-marked fever curve and other symptoms.
"n-a." ..... The same with milder symptoms.
"y-f." ..... Yellow fever about which particulars are not given, but not fatal unless so expressed.
"Alb." ..... Regular albuminuric yellow fever.
"alb." ..... The same of mild type.
"Hg." ..... Hemogastric yellow fever, with black or bloody vomit or melæna, of fatal termination.
"hg." ..... The same, not fatal.
"s." ..... Severe.
"f." ..... Fatal.
"m." ..... Mild.
"vm." ..... Very mild.

Symbol of contamination. The figures to the left of the oblique stroke express the days that have elapsed since the insects have bitten the infecting patient. To the right of the oblique stroke are expressed, in abbreviation, the type of the disease, and, in Roman numerals, the day of the attack when this patient was bitten.

Table I.—Inoculations with Recently Contaminated Mosquitoes.

No.	Inoculation.	Mosquitoes.	Contamination.	Result in first twenty-five days.	Ulterior yellow fever.	Subsequent residence.
1	30 June, 1881.	1	2 Hg., iv.	14 July, 1881, alb.	0.	4
2	22 July, 1881.	1	6 Alb., v.	27 August, 1881, abort.	0.	4
3						
4	31 July, 1881.	1	2 Hg., iii.	5 August, 1881, abort.	0.	4
5	2 August, 1881.	1	3 Hg., v.	17 August, 1881, eph.	0.	2
6	15 August, 1891.	1	2 Hg., vi.	0.	0.	4
7	7 August, 1891.	1	2 Alb., iii.	0.		
	11 September, 1881.	1	2 Hg., vii.	0.	10 September, 1882, N-a.	10
8	22 June, 1883.	2	2 Hg., vi.	9 July, 1883, N-a.	0.	10
9	15 July, 1883.	1	2 Alb., vii.	0		
	17 August, 1883.	1	2, 4 Hg., v.	26 August, 1883, N-a.	0.	12
10	15 July, 1883	1	2 Alb., vii.	0.		
	17 August, 1883.	1	2, 4 Hg., v.	0.	0.	3
11	21 August, 1883.	1	6, 8 Hg. v.	0.	5 June, 1884, hg.	3
12	16 July, 1883.	1	3 Alb., vii.	0.	0.	9
13	16 July, 1883.	1	2, 4 Alb., vii.	0.		
	18 August, 1883.	2	3 Hg. v.	9 September, 1883, alb.	0.	10
14	26 September, 1883.	2	2, 3 Alb., v.	0.	?	9
15	29 November, 1883.	1	3 Alb., iii.	0.	21 July, 1884, Hg.	x
16	29 November, 1883.	2	4 Alb., iv.	0.		
	30 May, 1884.	1	3 Hg., vi.	0.	7 August, 1884, y-f.	14
17	1 December, 1883.	1	4 Alb., v.	0.		
	6 May, 1884.	2	4 Alb., iv.	0.		
	23 February, 1887.	2	2 Alb., v.	0.	? July, 1890, y-f.	14
18	25 January, 1884.	1	? Hg., vi.	0.	?	?
19	16 June, 1884.	2	4 Hg., v.	0.	6 June, 1885, alb.	7
20	26 June, 1884.	1	3 Hg., v.	0.	28 September, 1884, Abort.	10
21	27 June, 1884.	1	3 Hg., v.	0.	23 November, 1884, N-a.	14
22	26 June, 1884.	1	3 Hg., iii.	0.	0.	14
23	28 August, 1884.	2	3 Hg., iv.	0.	0.	4
24	29 August, 1884.	2	4 Hg., v.	0.	0.	1
25	2 September, 1884.	1	2 Hg., iv.	0.	0.	4
26	27 August, 1884.	1	2 Hg., iv.	0.	0.	4
27	14 September, 1886.	1	? ?	0.	22 June, 1887, alb.	4
28	7 September, 1886.	1	6, 4 ?	23 September, 1886, N-a.	0.	5
29	14 September, 1886.	1	2 Hg., vi.	0.	0.	4
30	21 May, 1887.	1	2 Hg., vi.	0.	8 July, 1887, alb.	6
31	21 May, 1887.	1	2 Hg., vi.	0.	15 July, 1887, alb.	15
32	16 June, 1887.	2	2 Hg., iv.	11 July, 1887, alb.	0.	14
33	? July, 1887.	2	2 Hg., vi.	0.	? August, 1889, y-f.	14
34	11 September, 1887.	2	2 Alb., iii.	0.	17 September, 1893, Hg.	x
35	11 September, 1887.	2	2 Alb., iii.	0.	0.	4
36	13 September, 1887.	2	2 Alb., iv.	0.	0.	4
37	14 September, 1887.	2	2, 3 Alb., vi.	0.	0.	4
38	12 September, 1887.	2	3 Alb., ii.	0.	30 August, 1889, alb.	4
39	14 September, 1887.	2	3 Alb., vi.	0.	30 August, 1893, alb.	11
40	18 September, 1887.	2	2 Alb., vi.	0.	? August, 1888, N-a.	10
41	30 September, 1887.	1	3 Alb., vii.	0.	? January, 1889, Alb.	?
42	8 June, 1888.	1	3 Hg., iv.	1 July, 1888, N-a.	4 November, 1888, N-a.	14
43	12 September, 1888.	1	2 Alb., iv.	0.	18 June, 1890, n-a.	4
44	12 September, 1888.	1	2 Alb., iv.	0.	21 September, 1889, Abort.	3
45	22 October, 1888.	1	3 Alb., vi.	0.	0.	4
46	22 October, 1888.	1	3 Alb., vi.	0.	13 September, 1891, N-a.	4
47	23 October, 1888.	1	4 Alb., vi.	0.	23 September, 1889, n-a.	8
48	16 November, 1888.	1	2 N-a., ii.	0.		
	29 January, 1889.	1	3 Hg., iii.	0.	24 November, 1889, n-a.	8
49	16 November, 1888.	1	2 N-a., ii.	0.		
	28 January, 1889.	1	2 Hg., iii.	0.		
	26 April, 1889.	2	? Alb., iv.	0.	30 October, 1889, N-a.	7
50	16 November, 1888.	1	2 N-a., ii.	0.	? July, 1889, Abort.	4
51	11 April, 1889.	1	? Alb., v.	0.	0.	3
52	16 August, 1889.	2	3, Alb., iv.; Hg. v.	0.	10 September, 1892, N-a.	
					13 May, 1893, N-a.	4
53	16 August, 1889.	2	3 Alb., iv.	0.	16 August, 1893, alb.	5
54	16 August, 1889.	1	2 Alb., iv.	0.	0.	5
55	17 August, 1889.	2	3 Alb., iv.	26 August, 1889, Abort.	0.	5
56	16 August, 1889.	1	3 N-a., v.	0.	0.	5
57	22 May, 1890.	2	2 Hg., iii.	0.	17 November, 1890, N-a.	7
58	23 May, 1890.	2	2, 3 Hg., iii.	0.	0.	4
59	24 May, 1890.	2	3 Hg., iii.	0.	5 November, 1890, alb.	3
60	27 May, 1890.	2	7, 6 Hg., iii., v.	0.		
	13 October, 1890.	1	2 Hg., v.	0.	16 August, 1892.	5
61	13 August, 1890.	1	2, Alb., iv.	0.	0.	3
62	13 August, 1890.	1	2/Alb., iv.	0.	4 September, 1893, alb.	5

TABLE I.—INOCULATIONS WITH RECENTLY CONTAMINATED MOSQUITOES.—*Continued.*

No.	Inoculation.	Mosquitoes.	Contamination.	Result in first twenty-five days.	Ulterior yellow fever.	Subsequent residence.
63	13 August, 1890.	1	2/Alb., iv.	0.	14 September, 1898, alb.	3
64	13 August, 1890.	1	2 Alb., iv.	0.	0.	5
65	13 August, 1890.	1	2/Alb., iv.	0.	0.	7
66	14 August, 1890.	1	3/Alb., iv.	21 August, 1890, Abort.	4 July, 1895, Abort.	12
67	13 October, 1890.	1	2 Hg., iv.	0.		
	12 June, 1891.	1	2 Alb., v.	0.	19 September, 1895, Abort.	9
68	12 June, 1891.	2	2/Alb., iii.	0.	4 July, 1896, Hg.	4
69	15 June, 1891.	2	3 Alb., v.	0.	0.	3
70	15 June, 1891.	1	3/Alb., v.	0.	0.	3
71	16 June, 1891.	1	4, 3/Alb., iv.	0.	0.	5
72	16 August, 1891.	1	3, 2 Alb., iv.	0.	0.	5
73	16 August, 1891.	1	3, 2/Alb., iv.	0.	0.	3
74	16 August, 1891.	1	3, 2 Alb., iv.	0.	0.	5
75	16 August, 1891.	1	3, 2/Alb., iv.	0.	0.	5
76	25 August, 1892.	1	2 Hg., v.	0.	0.	4
77	27 August, 1892.	1	2/Hg., iv.	0.	8 September, 1893, Alb.	6
78	27 August, 1892.	1	2 Hg., iv.	0.	0.	1
79	17 April, 1893.	2	2/Hg., v.	0.	0.	5
80	17 May, 1893.	1	2/Alb., iv.	22 May, 1893, eph.	18 October, 1893, N-a.	
					26 August, 1895, hg.	5
81	28 May, 1893.	1	2/Alb., iv.	0.	20 September, 1893, n-a.	5
82	28 May, 1883.	1	2/Hg., iii.	11 June, 1893, eph.	1 September, 1893, hg.	8
83	17 June, 1893.	1	6, 3/Alb., v.	0.	23 November, 1893, Hg.	x
84	12 August, 1893.	1	3/Hg., v.	17 August, 1893, N-a.	0.	5
85	12 August, 1893.	1	2/Alb., iii.	0.	0.	1
86	12 August, 1893.	2	2/Alb., iii.	0.	0.	5
87	5 September, 1893.	2	2/Alb. vi.	0.	13 December, 1894, abort.	8
88	2, 3 December, 1893.	1	2/Hg., iv., v.	0.	25 February, 1894, Alb.	4
89	12 May, 1894.	1	4, 2/Alb., iv.	0.	17 September, 1895, eph.	3
90	6 June, 1894.	2	3/Hg., iv.	22 June, 1894, Abort.	18 August, 1895, Abort.	4
91	15 August, 1894.	2	2/Hg., iv.	0.	? February, 1898, y-f.	4
92	8 August, 1894.	1	3/Hg., vi.	0.	? June, 1896, y-f.	4
93	20 August, 1894.	1	2/Alb., iv.	0.	? June, 1896, y-f.	4
94	20 August, 1894.	1	2/Hg., iv.	0.	0.	4
95	20 August, 1894.	2	2/Alb., iv.	0.	0.	4
96	20 August, 1894.	1	2/Alb., iv.	0.	0.	4
97	21 August, 1894.	1	3/Alb., iv.	0.	0.	4
98	21 August, 1894.	1	3/Alb., iv.	0.	0.	4
99	8 December, 1894.	1	3/Hg., iv.	0.	14 July, 1895, alb.	4
100	19 January, 1895.	1	2/Alb., vi.	0.	18 July, 1895, Alb.	4
101	7 October, 1895.	1	3/Alb., ?.	0.		
	11 November, 1895.	1	4/Hg., viii.	0.	12 August, 1897, N-a.	6
102	2 September, 1896.	1	3/Hg., iv.	0.	0.	4
103	10 July, 1900.	1	2/Hg., vi.	0.	16 September, 1900, Alb.	3

my former tables) have been omitted, because the mosquito in those two cases had not previously bitten any yellow-fever patients.

I was fully aware, at the time, of the shortcomings in my mode of proceeding, the principal ones being: 1. That I had neither leisure nor other facilities for breeding my mosquitoes from the ova or from the larvæ, but had to rely on the outward appearance of the winged insects and on the conditions of the locality where they had been caught, in order to exclude as far as possible the chances that the insects might have been already infected at the time when they were caught. 2. That with the exception of one case (No. 9 of Table I.), in none of my cases had I been able to exclude altogether the possibility that the inoculated person might have been infected from some other source after my own inoculation. 3. That I could not assume the responsibility of attempting to produce severe, perhaps fatal experimental attacks by applying more than two or three recently contaminated insects at one time, or even one mosquito whose contamination dated back from several days or weeks, by either of which processes I had assumed that a dangerous experimental result might follow.

The outcome of my continued study had led me, in 1898, to the following conclusions:

1. That the germ of yellow fever is only pathogenous for human beings when introduced by inoculation. 2. That the regular process by which the inoculation of the germ is accomplished, in nature, is through the bites of the culex mosquito (Stegomyia fasciata Theo.), the insect having previously become contaminated through the act of biting a yellow-fever patient within the first five days of his attack. 3. That although the bites of a recently contaminated mosquito can produce at most only a very mild attack of yellow fever, or simply confer latent immunity without eliciting any obvious pathogenic manifestation, the bites of the same insect, when its contamination dated back from several days or weeks, might produce severe or fatal attacks. 4. That the yellow-fever mosquitoes, after they have once become contaminated, retain the power of inoculating the disease during the rest of their lives. 5. That yellow fever might be stamped out of Havana by just such a method as the one which was adopted by Major W. C. Gorgas, with signal success, in 1901.

EXPERIMENTAL DEMONSTRATION OF THE MOSQUITO THEORY AND NEW FACTS BROUGHT TO LIGHT BY THE UNITED STATES ARMY YELLOW-FEVER COMMISSION * IN HAVANA.

A most eventful period in the history of yellow-fever investigation opened in the month of July, 1900, when the yellow-fever commission, which had been sent from Washington to study that disease in Havana, undertook to investigate the mosquito theory of yellow-fever transmission with a brood of those insects developed from ova of the culex mosquito (Stegomyia fasciata Theo.) which I had preserved and placed at their disposal.

In the course of twenty days, from August 11th to 31st, 1900, they tried the mosquito inoculations upon eleven non-immunes. The results were negative in their first nine attempts, which consisted in applying to a non-immune one or two insects which had bitten a case of yellow fever (mostly of a mild type) two, three, four, five, six, eight, or thirteen days before biting the non-immune. Their next two attempts, however, proved successful beyond their expectations. The first of these

* This commission was composed of Walter Reed, M.D., Surgeon, U. S. A., James Carroll, M.D., and A. Agramonte, M.D., Jesse W. Lazear, M.D., Acting Surgeons, U. S. A. Dr. Lazear died of yellow-fever while Dr. Carroll was barely convalescent of his experimental attack. He attributed his own attack to the circumstance that during a visit to the yellow-fever ward of Las Animas Hospital, four or five days before he was taken sick, he had noticed a mosquito biting his hand, and being already a believer in the mosquito theory he had refrained from driving away the insect and had allowed it to fill itself completely in order to watch the result.

was made upon a member of the commission, Dr. Carroll, who applied to his own arm a mosquito which had bitten four yellow-fever patients (two of them severe cases) two, four, six, twelve days before the inoculation. Three days and seven hours after the bite of the contaminated mosquito, Dr. Carroll was taken sick with a severe attack of well-characterized albuminuric yellow fever (see No. 1, Table II.). The second successful inoculation was obtained upon a non-immune American, who offered himself for the trial. He was bitten by four mosquitoes which, between them, had previously bitten ten yellow-fever patients (two of them fatal and two severe ones) at different intervals varying between two and sixteen days before the inoculation. This American was attacked at the end of six days and two hours with high fever, and presented all the characteristic symptoms of yellow fever, the albuminuria and jaundice continuing till several days after convalescence (No. 2 of Table II.).

In neither of these two cases had the inoculated subjects been isolated or kept under close observation until the first symptoms of the attack had declared themselves; but the circumstance that their insects were home-bred, that the attack had commenced within the classical limits of the yellow-fever incubation, and that the symptoms were very characteristic, convinced them not only of the fact that the mosquito was indeed the transmitter of the disease, but also, by reason of their first negative results, that an interval of at least ten or twelve days must elapse after the insect has bitten a yellow-fever patient before it acquires the faculty of inoculating the disease. They decided, therefore, to act in accordance with this principle in all their future experiments.

After delivering their preliminary report with a minute account of their two successful inoculations, the same commission returned to Havana with instructions to carry out to a close the demonstration of the important question involved: Whether or not the Stegomyia mosquito is the natural transmitter of yellow fever. For this purpose they were provided by Gov.-Gen. L. Wood with ample means, and permitted to repeat their mosquito inoculations upon any non-immune who, after being informed of the risks, should consent to be experimented upon.

After a careful preparation of the premises and the adoption of many ingenious devices to exclude chances of error, the commission started a series of mosquito inoculations which, under the circumstances in which they were performed, left no room for a doubt as to the fact that the experimental attacks which followed the inoculations could be attributed only to the bites of their contaminated mosquitoes.

By adhering to the rule of using in their experiments only mosquitoes having more than ten or twelve days of contamination, and which had been kept at summer temperatures (80° to 82° F.), they had no difficulty in obtaining well-marked results, the failures having been the exception. They were thus able to contaminate their fresh mosquitoes from previous experimental cases of their own, and, on some occasions, to confirm a doubtful clinical diagnosis by applying to a non-immune mosquitoes which had bitten the patient.

The fourteen successful mosquito inoculations obtained by the Army Board during the years 1900 and 1901 have been tabulated for future references (see Table II.), leaving their other valuable experiments with the injection of yellow-fever blood, and others also for the purpose of demonstrating that fomites and air-borne germs have no share in the propagation of the disease, to be considered after I have completed the record of all the inoculations with mosquitoes that have so far been published.

Table II.—Successful Mosquito Inoculations by the United States Yellow-Fever Board, 1900 and 1901.

No.	Subject.	Inoculation.	Mosquitoes.	Contamination.	Incubation.	Experimental Attack.
1	Dr. C.	27 August, 1900	1	12/4/s., ii. 6/2/m., ii.	3 days 7 hours	August 31: s. Alb.
2	X.	31 August, 1900	4	12/f., i., ii. 12/16/6/4/2/s., i., ii. 10/6/2/m., i., ii.	6 days 2 hours	September 7: Alb.
3	J. R. K.	5 December, 1900	5	15/f/i., 19/s., ii. 21/m., ii.	3 days 9 hours	December 9: Alb.
4	Sp. a.	8 December, 1900	4	17/f., iii., 19/22/s., iii. 24/m., iii.	5 days 17 hours	December 14: alb.
5	Sp. b.	9 December, 1900	1	19/f., ii.	3 days 11 hours	December 12: alb.
6	Sp. c.	11 December, 1900	4	20/f., iii. 25/s., iii. 27/m., iii.	3 days 10 hours	December 15: alb. tr.
7	Sp. d.	21 December, 1900	?	Mosquito house.	3½ days ?	December 25: alb.
8	Sp. e.	30 December, 1900	4	17 (case 5), i.	3 days 22 hours	January 3: alb.
9	L. F.	19 January, 1901	3	39/s., iii.	4 days	January 23: Alb.
10	C. W.	31 January, 1901	2	51/s., iii.	3 days 2 hours	February 3: alb. tr.
11	J. H.	6 February, 1901	2	57/s., iii.	3 days 6 hours	February 9: Alb.
12	C. S.	7 February, 1901	3	16/f., ii.	2 days 22 hours	February 10: N.-a.
13	Sp. f.	16 September, 1901	4	53/f., iii. 34/f., ii.	3 days	September 10: Alb.
14	Sp. g.	9 October, 1901	8	18/(case 13), ii.	3½ days	October 13: alb. tr.

The following series of Prof. John Guiteras will show the advantage of including in such reports not only the successful experiments, but also the negative ones.

During the spring and summer of 1901 Professor Guiteras, being in charge of the Experimental Station at Las Animas Hospital, undertook to ascertain whether the mosquito inoculation could be safely used as a means of conferring immunity upon new comers. His experiments at Las Animas were performed according to the rules set down by the Army Board, and the same precautions were taken to exclude sources of error. In the course of nine months, from February to October, 1901, he performed forty-nine inoculations upon twenty-three subjects who were supposed to be non-immunes, but two of them apparently were not. Nine of the forty-nine attempts were followed by a well-marked attack of yellow fever within three to six days after the bites of the infected mosquitoes. The first successful inoculation (No. 2, Table III.) was performed with a mosquito which had been presented to me by Dr. Carroll, of the Army Board, and which had bitten only once an experimental blood case (No. 4, Table IV.) about nine hours after the invasion. This insect was applied on the 23d of February to a non-immune Spaniard who was taken sick on the 26th at midnight with a mild but characteristic attack of albuminuric yellow fever (No. 2, Table III.).

Seven of Dr. Guiteras' successful inoculations were obtained with mosquitoes which had been contaminated from a particular patient (Alvarez), while other mosquitoes which had bitten different yellow-fever patients coming from the same locality, and who had been attacked about the same time as Alvarez, all gave negative results, even when applied to subjects who afterward succumbed to the Alvarez mosquitoes. The attack in the infecting patient (Alvarez), though severe, had not been fatal; yet the insects which had bitten him only once acquired such a virulent contamination that out of

TABLE III.—MOSQUITO INOCULATIONS PERFORMED BY PROF. J. GUITERAS AT LAS ANIMAS EXPERIMENTAL STATION, HAVANA, 1901.

No.	Name.	Inoculation.	Mosquitoes.	Contamination.	Result.	Incubation.
1	Gross	(a) 22 February	1	13/? iii.	0	
		(b) 17 March	1	17/(No. 2), ii.	0	
		(c) 14 April	1	15/vm., ii.	0	
		(d) 2 June	3	19/vm., ii.	0	
2	Vergara	23 February	1	26/(4, Table IV.), i.	Alb. y-f.	3 days 10 hours.
3	Quintillan	8 March	1	9/vm., iv.	0	
4	Maas	(a) 17 March	1	17/(No. 2), ii.	0	
		(b) 25 March	1	25/(No. 2), ii.	0	
		(c) 16 May	3	6/m., ii.	0	
		(d) 27 May	4	18/m., ii.	0	
		(e) 4 June	4	26/m., ii.	0	
		(f) 15 August	2 Alv.	24/hg., iii.	Fatal Hg.	3 days 21 hours.
5	Martinez	26 March	1	25/m., ii.	0	
6	Represas	(a) 17 March	1	18/m., ii.	0	
		(b) 31 March	1	25/m., ii.	0	
		(c) 8 August	4 Alv.	19/hg., iii.	Severe hg.	3 days 3 hours.
7	Santiso	(a) 30 April	1	21/m., ii.	0	
		(b) 16 May	2	7/m., ii.	0	
		(c) 2 June	3	20 vm., ii.	0	
8	Carro	(a) 25 April	1	25/m., ii.	0	
		(b) 24 May	4	15/m., ii.	0	
		(c) 8 August	4 Alv.	19 hg., iii.	Fatal hg.	4 days 5 hours.
9	Taylor	(a) 1 May	3	9 m., ii.	0	
		(b) 8 May	3	17/m., ii.	0	
		(c) 15 May	2	23/m., ii.	0	
		(d) 29 May	3	20/m., ii.	0	
		(e) 7 June	4	24 m., ii.	0	
		(f) 7 August	5	20/m., ii.	0	
		(g) 13 August	1 Alv.	24/hg., iii.	Alb. y-f.	3 days 14 hours.
10	Vazquez	31 May	4	22/m., ii.	0	
11	Campa	(a) 31 July	4	5/Hg., iii.	0	
		(b) 9 August	3 Alv.	20/hg., iii.	Fatal Hg.	5 days 3 hours.
12	Martin	(a) 4 August	4	17/m., ii.	0	
		(b) 13 August	2 Alv.	24/hg., iii.	0	
13	Varela	(a) 4 August	4	17 m., ii.	0	
		(b) 14 August	3 Alv.	24/hg., iii.	Severe y-f.	5 days 21 hours.
14	Holmes	(a) 7 August	1	14/hg., iii.	0	
		(b) 8 August	1	15/hg., iii.	0	
15	Migues	10 August	2	22/m., ii.	0	
16	Thomlison	10 August	2	22/hg., iii.	0	
17	Dominguez	10 August	4	15/Hg., iii.	0	
18	Alonso	24 August	2 Alv.	34/hg., iii.	Severe hg.	3 days.
19	Vicente	24 August	2 Alv.	36/hg., iii.	0	
20	Seuil	17 November	1	57/(13, Table II.), ii.	Alb. y-f.	4 days 2 hours.
21	Rivero	(a) 17 November	1	26/(No. 1, Table VI.), ?	0	
		(b) 19 December	1	23/(No. 20, Table III.), iv.	0	
22	Kirby-Smith	28 November	1	3/(No. 20, Table III.), iv.	0	
23	Lopez	(a) 28 November	1	3/(No. 20, Table III.), iv.	0	
		(b) 15 December)	1	16/(No. 20, Table III), iv.	0	

TABLE IV.—EXPERIMENTAL YELLOW FEVER PRODUCED BY THE ARMY BOARD WITH THE INJECTION OF BLOOD FROM YELLOW-FEVER PATIENTS, 1901.

No.	Name.	Injection.	Quantity.	Source.	Attack.	Incubation.
1	W. J.	January 4th, 1901	2.0 c.c.	(m., y-f), ii.	January 8th: Alb.	3 days 22 hours.
2	W. O.	January 8th	1.5 c.c.	(No. 1, T. IV.), i.	January 11th: m. y-f.	2½ days.
3	W. F.	January 22d	.5 c.c.	(f. Hg.), ii.	January 24th: s. Alb.	1 day 19 hours.
4	J. H. A.	January 25th	1.5 c.c.	(No. 3, T. IV.), ii.	January 28th: Alb.	3 days 8 hours.
5 ?	J. M. B.	October 22d	1.5 c.c.	(No. 1, T. VI.), iv.	October 23d ?	24 hours.

Case 5 received an injection of filtered serum on the 15th and another of fresh blood on the 22d; opinions being divided as to which of the two injections was the successful one, the case has been recorded with a query, both in this table and in the following one (No. 3 ? T. V.).

nine persons to whom they were afterward applied seven were attacked with severe yellow fever, and three of them proved fatal. A mosquito which had been fed from the arm of Dr. Guiteras' first experimental case (No. 2, Table III.) gave a negative result when applied after seventeen days, and again eight days later, with twenty-five days of contamination, to Miss Maas (No. 4, *a* and *b*, Table III.), who died three months later from the bites of two of the Alvarez mosquitoes (No. 4, *f*, Table III.). Another mosquito which had bitten the patient upon whom Dr. Carroll had experimented with unheated defibrinated blood (No. 1, Table VI.), was applied, twenty-six days after biting this patient, to a non-immune (No. 21 *a*, Table III.) with a completely negative result. Finally, three mosquitoes which had bitten Dr. Guiteras' last successfully inoculated patient (No. 20, Table III.) three days and five hours after the first onset of the fever, were applied at the end of three, sixteen, and twenty-three days respectively to three non-immunes (No. 22, 23 *a* and *b*, 21 *b*), and the result was negative in all three. These results evidently prove that not all the Stegomyia mosquitoes that bite genuine yellow-fever patients become infected, even when all the conditions set down by the Army Board are complied with. This had already been inferred by Dr. Reed after witnessing an instance in which the simultaneous bites of twelve mosquitoes which had bitten a mild experimental case (No. 8, Table II.) failed to transmit the disease to a person considered non-immune, although the injection of 2 c.c. of blood drawn from the same patient had produced a characteristic attack in another non-immune (No. 1, Table IV.). The only hypothesis which affords a satisfactory explanation of these apparent anomalies seems to be that many of the natural or experimental cases of genuine yellow fever, but principally among those of a mild type, are due to the introduction of a limited number of germs which, having taken root, as it were, in some undetermined region of the body, establish a localized infection; and that the general symptoms of yellow fever which follow are elicited by the soluble toxins

conveyed through the blood circulation. Under these circumstances mosquitoes fed from the germ-free peripheral blood would not become infected, while a direct injection of the blood itself, saturated with toxins, might produce a purely toxæmic attack of yellow fever insusceptible of further reproduction.

The importance of this hypothesis will be better appreciated after one has gone over the interesting and highly instructive experiments which were performed by the Army Board with blood freshly drawn from the general circulation of yellow-fever patients on the first or second day of their attack.

Their first series consisted in injecting subcutaneously from 0.5 to 2 c.c. of blood drawn from a vein in the arm of a yellow-fever patient. They have reported five successful experiments of this kind (Table IV.), but the fifth, as will be explained farther on, belongs more properly to their other experiments with filtered blood serum (Table V.), and has for that reason been included in both tables, with a query appended to each.

The conclusions of the Army Board regarding their blood inoculations were expressed in the following terms: "First, that the parasite is present in the blood—at least during the early stages of the disease; secondly, that the passage through an intermediate host is not essential in the life cycle of the parasite. Thus yellow fever is analogous to the malarial fevers in that it may be produced either by the bite of a certain species of mosquito or by injection of blood taken from the general circulation." (*American Medicine*, July 6th, 1901, p. 16.)

Another very important investigation was carried out by the Army Board with blood drawn from a vein at the bend of the elbow of a mild experimental case (No. 14, Table II.). This blood, amounting to 65 c.c., was placed in a sterile test tube and set aside during five and one-half hours in the refrigerator. At the end of that time 19 c.c. of the supernatant, slightly blood-stained serum was pipetted off into another sterile tube, and after diluting it with an equal quantity of sterilized distilled water, it was filtered through a Berkefeld filter, previously tested and sterilized. Ten and a half hours after the blood had been drawn from the patient, 3 c.c. of the filtrate, corresponding to 1.5 undiluted serum, was injected into two American non-immunes (Nos. 1 and 2, Table V.). had been observed at the end of the seventh day, and the same subject was again utilized for another experiment. He was injected, at the commencement of the eighth day since his previous injection with filtered serum, with 1.5 c.c. of blood freshly drawn from the arm of the first American (No. 1, Table V.) on the fourth day of the attack. The object of this blood injection had been to ascertain whether the experimental attack in No. 1 (Table V.) should be attributed to soluble toxins contained in the filtered serum, in which case the second injection must be expected to give a negative result, or to the presence of ultra-microscopic germs which had passed through the Berkefeld filter, and which, having multiplied after being inoculated, would enable the disease to be reproduced through the injection of the patient's blood. This well-conceived experiment was, however, deprived of its significance by the circumstance that, not having at hand a fresh non-immune, it was performed upon a subject who might still be under the influence of a previous experiment. In point of fact, exactly eight days after this third American had received the injection with filtered serum, and just twenty-four hours after his injection with the fresh blood (No. 3, Table V., and No. 5, Table IV.), he was attacked with a mild form of yellow fever, showing a trace of albumin on the fourth day. The question as to which of the two injections had been the successful one rests, therefore, on the greater probabilities of an incubation period of eight days rather than of one of twenty-four hours. The experimenters decide in favor of the latter, but I cannot agree with them on that decision, for there is no reliable precedent for such a brief incubation as twenty-four hours in the records of either natural or experimental cases, while there are examples of both kinds regarding an incubation of eight days. Dr. Carter, in his valuable paper on that subject (New York *Medical Record*, March 9th, 1901, p. 366), gives the particulars about four members of a family who at different hours of the same day had gone from a non-infected house where they lived to an infected one at a short distance from their home, and they were all taken sick with yellow fever in the course of the eighth or ninth day after that visit, while a fifth member of the family who had not accompanied the others in their visit to the infected house, only took the disease several weeks later. As an experi-

TABLE V.—EXPERIMENTAL YELLOW FEVER WITH INJECTION OF 1.5 C.C. OF FILTERED BLOOD SERUM FROM CASE (No. 14, TABLE II.) IV.

No.	Name.	Injection.	Time *in vitro*.	Attack.	Incubation.
1	P. H.	October 15th.	10½ hours.	m., y-f., tr., alb.	4 days 4 hours.
2	W. C.	October 15th.	10½ hours.	abort., y-f., no alb.	4 days 1 hour.
3 (?)	J. M. B.	October 15th.	14 hours.	vm., y-f., tr., alb.	8 days.

NOTE.—Case 3, see note to Table IV.

TABLE VI.—COMPARISON BETWEEN UNHEATED BLOOD AND THE SAME BLOOD AFTER HAVING BEEN HEATED TO 55° C., DURING TEN MINUTES, WHEN INJECTED INTO NON-IMMUNES

No.	Name.	Injection.	Source.	Quantity.	Condition.	Result.
1	(Control) M. G. M.	October 15th.	(14 Table II.) iv.	0.75 c.c.	Unheated.	m., y-f., tr., Alb., October 20th.
2	Sp. A. C.	October 15th.	(14 Table II.) iv.	1.5 c.c.	Heated.	0.
3	Sp. R. F. M.	October 15th.	(14 Table II.) iv.	1.5 c.c.	Heated.	0.
4	Sp S. O.	October 15th.	(14 Table II.) iv.	1.5 c.c.	Heated.	0.

Both fell sick, after an incubation of a little over four days, with a mild attack of yellow fever. One showed a trace of albumin on the fourth day, but the other had none at all during his entire illness. The latter was, in fact, a type of what I have elsewhere termed the non-albuminuric abortive form. Three and a half hours after the inoculations of these two Americans, a third one (No. 3, Table V.) was likewise injected with the same quantity of the filtered serum, which by that time had been kept fourteen hours in the refrigerator. This inoculation was thought to have been a failure, as no reaction

mental case in point, I can quote the only one (No. 9, Table I.) of my one hundred and two inoculated subjects about whose isolation from other sources of infection I had a reliable guarantee. With regard to the mosquito which I had used, it was not a home-bred insect, so that I have not the same certainty that it might not have bitten a yellow-fever patient before it was caught; but at any rate, I do know that the only source of infection to which the person had been exposed was the bite of my infected mosquito. He was bitten on the 17th of August, 1883 (hour not recorded), and was taken sick on

the 26th at 11 45 A.M., with a characteristic attack of non-albuminuric yellow fever, only a doubtful trace of albumin having been obtained in the night of the fourth day. There were hawking up of bloody phlegms, bleeding from the gums on pressure, yellowness, and the spontaneous defervescence on the seventh day, and his immunity was subsequently proved by more than twelve years of residence in Havana. In this experimental case, therefore, the incubation was between eight and nine days.

Until some more decisive experimental proof can be given, I must therefore adhere to my belief that the pathogenic effects which followed the injection of filtered blood serum in the experiments by the Army Board were due to the soluble toxins contained in that serum rather than to the hypothetical ultra-microscopic germ invoked by the experimenters. I believe, furthermore, that those experiments confirm my opinion about my own experimental cases (see Table I.), and that some of the pathogenic effects, which were observed after a few of my inoculations with recently contaminated mosquitoes, may have been due to the direct inoculation of human germs which had been retained upon the setæ of the insect's sting; these germs having found an appropriate nesting-place in some region of the body of the inoculated person and producing through their toxins mild non-infectious attacks of yellow fever, such as I have mentioned in connection with Dr. Guiteras' experiments at Las Animas.

While the inoculations with filtered serum were being carried on by the Army Board, the residual blood which had remained in the test tube after the supernatant serum had been pipetted off was mixed with 19 c.c. of sterilized distilled water and beaten up with a sterilized egg-beater, to remove most of the fibrin. This mixture may be supposed to have differed from the original 65 c.c. of blood, in that it would be poorer in soluble toxins by the quantity contained in the 19 c.c. of supernatant serum which had been pipetted off, but richer in living germs, for these would naturally gravitate, together with the red globules, to the bottom of the test tube. Fifteen and a half hours had elapsed since the blood had been drawn from the patient (five and a half in the refrigerator and ten at room temperatures) when they injected 0.75 c.c. of the above mixture into a non-immune Spaniard who was attacked, at the end of five days and two hours, with a mild but characteristic yellow fever showing a trace of albumin on the fourth day. In the mean time another portion of the same blood mixture was subjected during ten minutes to a heat of 55° C., and of this heated portion, after it had been cooled down, 1.5 c.c. were injected into three non-immune Americans, with a completely negative result, "no rise of temperature nor other symptoms of ill-health having followed the injection."

The outcome of these important experiments seems to be that the yellow-fever germ is killed by ten minutes' exposure to 55° C., but is not entirely deprived of its virulence by exposure to the cold of a refrigerator (presumably between 40° and 50° F.) during five and a half hours, nor by being kept *in vitro* fifteen and a half hours after having been drawn from the human subject. The soluble toxins contained in the filtered serum, on the other hand, appear to lose some of their virulence when kept beyond ten hours in the refrigerator; but nothing is known about their susceptibility to heat.

The original finding of the Army Board that through the bites of the insect variously named Culex mosquito Desv., Culex fasciatus Fab., Stegomyia fasciata Theo., experimental attacks of yellow fever can be produced almost at will has now, therefore, been established beyond the possibility of a doubt. But the Board had yet another task to fulfil, namely, to show that the disease is not also transmitted by any of the other modes of contagion which had formerly been invoked. For this purpose they instituted two very convincing experiments. One consisted in partitioning a room, by means of mosquito-proof wire netting, into two compartments, so that a certain number of contaminated mosquitoes which had been introduced into one of the compartments could be seen from the other side of the screen, but could not cross the barrier. A non-immune was then introduced on three occasions on two successive days into the compartment with the contaminated insects, while at the same hours two other non-immunes occupied the compartment on the other side of the screen. At the end of three days and twenty-three hours from his first visit to the mosquito compartment the first of these non-immunes was taken sick with a characteristic attack of yellow fever, while neither of the two who had been in the mosquito-proof compartment experienced the slightest inconvenience.

The other experiment consisted in accumulating in a mosquito-proof building constructed *ad hoc* all sorts of garments, bedding, rags, and refuse which had been soiled or used by yellow-fever patients or by their discharges, under the worst imaginable conditions, and allowing three non-immunes not only to enter that building, but to handle the objects, and to unpack them out of the boxes in which they had been preserved, to sleep in the soiled beds, etc., during twenty successive days. This performance was again gone through by two other couples of non-immunes during the two following periods of twenty days, and yet none of the seven who were thus exposed suffered the slightest disturbance in their health.

In order to try whether the local influence had contributed to these negative results, Major J. Ross, United States Navy, as director of Las Animas Hospital, repeated the same experiment some months later at this hospital, and the results were equally negative.

The universal conviction which has now been reached as to the fact that the mosquito does transmit yellow fever has given rise to the suggestion that other blood-sucking insects should also be able to do so. That this is not the case must be directly inferred from the circumstance that most of the blood-sucking insects, apart from the Stegomyia fasciata (Culex mosquito Desv.), are common to localities where yellow fever is transmissible, and to others where it is not transmitted from the sick to the healthy. In point of fact the difficulty in the study of yellow-fever etiology has not been to find an agent which should transmit the disease indiscriminately, but, on the contrary, to account for the fact that the disease has a very limited geographical distribution, and that its propagation is markedly affected by local conditions which are not known to affect in an equal degree any other blood-sucking insect but the Culex mosquito.

Deductions from the Experimental Facts that have been Recorded.—1. Only two ways are known by which yellow fever can be experimentally transmitted from a yellow-fever patient to a non-immune: one is through the bites of Stegomyia mosquitoes which have previously bitten a well-marked case of yellow fever within the first days of his attack, and which have been kept at summer temperatures (80° to 82° F.); and the other through the injection of blood or blood serum collected from a yellow-fever patient, also within the first days of his attack. In nature, only the first of these processes can occur.

2. Other modes of infection through fomites, both while fresh and after having been kept during several months, have proved ineffectual as a means of reproducing the disease.

3. While severe cases of yellow fever appear, as a rule, to be infectious for yellow-fever mosquitoes that have been kept at summer temperatures, not a few of the mild cases seem to be incapable of infecting those insects, even when the injection of blood collected from the same patient does occasion a mild attack.

4. The occurrence of attacks of yellow fever which cannot infect mosquitoes suggests a localized infection in some undetermined region of the body, within the boundaries of which the germs remain confined. The general symptoms would then be due to the soluble toxins conveyed through the general circulation, so that an injection of this sterile blood, saturated with toxins, might yet develop a purely toxæmic attack insusceptible of further reproduction, while mosquitoes fed with the same blood would not become infected.

5. Non-infectious forms might follow the bites of recently contaminated mosquitoes, when the live germs retained upon the setæ of the insect's sting are deposited in the wound inflicted with its next bite, and find an appropriate nesting place in which a local infection may be originated.

6. The more acute course observed in the experimental cases produced with the blood injection, as compared with those resulting from the bites of moquitoes, may be due to the fact that with the former not only the live germ, but also the soluble toxins are injected, while the mosquito bite cannot be expected to convey any of the human toxins.

7. Table VI. shows that the yellow-fever germ is killed by ten minutes' exposure to a heat of 55° C., but not by exposure to low temperatures in a refrigerator during five and a half hours, nor by being preserved in vitro during fifteen hours. Table V., on the other hand, suggests that the soluble toxins lose some of their virulence when they have been kept in vitro beyond ten hours at temperatures between 40° and 50° F. (in a refrigerator).

8. The immunity acquired by foreigners after long residence in yellow-fever countries, without ever having suffered an attack of the disease, is probably due to repeated inoculations with recently contaminated mosquitoes, such as I have recorded in Table I.

Distinctive Features and Habits of the Yellow-Fever Mosquito.—The yellow-fever mosquito is the regular day mosquito by which all the houses in Havana are infested during the summer season, and even during winter some are habitually seen flying about and ready to bite whenever the temperature rises above 75° F. It remains hidden or asleep during the night hours unless disturbed in its rest by the admission of artificial light; but is wide awake, on the contrary, from daybreak till night-time. They are more abundant, however, at some hours than at others.

The yellow-fever mosquito has been included among a group of gnats variously named by their discoverers and some of which present more or less marked differential characters, but having in common the peculiar scale arrangement upon the nape and scutellum that characterizes Theobald's new Stegomyia fasciata species. Without calling into question the scientific grounds for this classification, it may be doubted whether all the members of the group possess the faculty of reproducing yellow fever, inasmuch as the regular habitat of yellow fever is confined to the intertropical zone of the Atlantic ocean, while the geographical distribution of the entire Stegomyia fasciata species is said to extend over almost all the lowlands of the tropical and intertropical belt around the globe. The only variety of that species which has so far proved capable of transmitting yellow fever was named Culex mosquito by Robineau Devoidy and agrees in all respects with Ficalbi's description of his Culex elegans. The characters by which, as a tyro entomologist, I was able to differentiate it from the night mosquito of Havana, and also from another day mosquito which occasionally makes its appearance in the same city, were the following ones: Its graceful form and agility of movements; dark gray, sometimes almost black color of its body with silver or snow-white ornamentation; white rings around the five last joints of its hind-legs—three upon those of the middle legs, and two upon the front ones; ventral segments of the abdominal rings of a dirty white; sides of the abdomen presenting a double row of white dots; sides of the thorax ornamented with several white patches of irregular outline; front view of the thorax from above presents a combination of white lines figuring a two-stringed lyre, the two parallel lines corresponding to the strings having at times a slight golden tinge; the face presents three white spots forming between them a symmetrical triangle pointing downward; the proboscis is uniformly black, but when the white tips of the palps (in the female) are resting on the upper part of the sheath, they may be mistaken for markings on the proboscis. The shortness of the wings in the yellow-fever mosquito struck me as a very convenient differential feature; when closed they leave the last segment of the body uncovered; in the night mosquito (C. pungens or pipiens?) they are just long enough to cover the posterior end of the body; while in the other day mosquito referred to above, and which resembles the night mosquito in many respects, the wings when closed project beyond the posterior end of the body. The yellow-fever mosquito has a peculiar way of laying its ova, not in the shape of a neat boatlet, like the night mosquito, nor in an irregular lump like the other day mosquito, but singly, in rows, or irregularly disposed upon the surface of the water or upon the walls of the receptacle above the water-line.

With the yellow-fever mosquito, as with the generality of gnats, it is only the female that bites and sucks blood. It disappears from view when the temperature falls below 70° F., hiding, in a state of semi-hibernation, in dark corners, behind presses or book-shelves, etc., but comes out again, anxious to bite, when the temperature rises to between 70° F. and 80° F. The shortest interval between two successive bites, when the insect has had a full meal of blood, is forty-eight hours in the hot season, but when the temperature is cool the interval may extend to five or six days. Ovulation is to a great extent regulated by the opportunities which the insect has had of biting and sucking blood. As a rule, it does not bite before having been fecundated; one fecundation proves, however, sufficient for all the ova that are to be laid by a female. All the ova are not laid in one batch, but at different intervals, a new feed of blood being apparently necessary for every new batch. The natural longevity of the female insect varies considerably under different circumstances, and even when several are caged together some may be short-lived, while others attain an old age. Probably the circumstance of not being allowed to bite, so that all their ova cannot be laid, may tend to prolong the term of their lives. In the condition of semi-hibernation which is produced by a temperature of 40° to 50° F., Dr. Guiteras informs me that he has had under observation Stegomyia mosquitoes which have reached the age of two and a half months, without any food and with no other water supply but the droplets condensed upon the walls of the cage. A contaminated mosquito which had never been allowed to bite after its contamination lived at room temperatures upon sugar and with a provision of water, five months (from August to December, 1902). In their natural condition, however, even without taking into consideration their numerous exposures to violent death, I imagine that the yellow-fever mosquito seldom lives beyond forty or fifty days in the summer season. They have, moreover, many natural enemies, some of which attack them in the larval stage, as do the larvæ of the Psorophora, and others also as a winged insect. The yellow-fever mosquito is killed by temperatures above 40° C.

For a more technical account of the Stegomyia fasciata the reader must be referred to Prof. H. B. Ward's article on *Mosquitoes in Relation to Human Pathology* in Volume V. of this HANDBOOK.

PROPAGATION OF YELLOW FEVER.

A recognition of the fact that yellow fever can be transmitted in nature only through the agency of the contaminated Stegomyia mosquito leads to the following conclusions:

When a case of undoubted yellow fever originates in a locality known to have been free from the disease during a certain length of time, including several months of summer temperatures, in a person who has not absented himself from the locality during the last ten or fifteen days previous to his illness, one of three events must be supposed to have happened.

1. If in the locality considered the Stegomyia mosquito does not exist, one or more mosquitoes of that species having had opportunities for biting yellow-fever patients must in some way have been introduced and had access to the first person attacked with the disease. The incrim-

inated insect must have become infected since at least ten or twelve days, but possibly as far back as several months, before biting the new case on hand, and the latter was probably bitten by the contaminated mosquito between three and nine days before he was taken sick.

2. If the yellow-fever mosquito is a normal dweller in the locality which we are considering, there is a possibility that an unrecognized yellow-fever patient, within the first days of his illness (perhaps a passenger in a railway train stopping a few moments in the city station, on a ferry, or in any other conveyance) may have been bitten incidentally by one of the local Stegomyia mosquitoes, so that after the lapse of a couple of weeks cases of yellow fever may begin to develop in the locality.

3. Contaminated mosquitoes may be introduced with an immature contamination, so that the first non-immunes who happen to be bitten by them will not take the disease while, a few days later, every non-immune who is bitten by the same insects will be likely to be attacked with yellow fever within the week following the bite.

Manner in which Contaminated Mosquitoes may be Conveyed from One Place to Another.—The most obvious modes of conveyance include the casual imprisonment of contaminated insects inside of trunks, boxes, parcels, etc., and it sometimes happens that a mosquito is entrapped under a hat at the moment when it is actually biting the wearer's head. Within certain variable limits of time, in accordance with what has been said regarding the longevity of the yellow-fever mosquito, the contaminated insect may be restored to liberty when the trunk or the box comes to be opened, or the first time the wearer of the hat uncovers his head; and thus the foundation for an epidemic may be laid. The mosquito, as a rule, does not fly away to any distance from the dwelling where it has established itself; but it may wander away the length of one or two blocks in pursuit of a victim or when driven from its quarters by obnoxious fumes such as are developed in disinfecting a house or a room, if the retreat of the infected insects has not been cut off. With its short wings the yellow-fever mosquito is incapable of supporting itself in the air when a strong wind is blowing. Under these circumstances, if carried away by the wind from the deck of a ship, or from the shore, it might strive to save itself from drowning by alighting upon some floating object, which, drifting with the current, would perhaps land the insect at a greater distance than it could have reached flying. Vessels trading with ports in the yellow-fever zone are apt to be boarded by the Stegomyia mosquito, and new broods of that species may be developed in the water tanks or barrels, or in accidental collections of stagnant fresh water in any part of the ship. Fruit vessels or those laden with sugar must be particularly attractive to these insects. Thus it is evident that without any actual imprisonment the Stegomyia may make its temporary or permanent home in vessels as well as in public conveyances, railway carriages, freight cars laden with fruit, etc., when the local conditions are favorable. In the presence of so many sources of danger it must, therefore, be recognized that our only chance of actually controlling the propagation of yellow fever lies in our ability to carry out the following precepts:

1. To protect yellow-fever patients from the bites of mosquitoes.

2. To prevent the escape of any of the mosquitoes that have bitten a yellow-fever patient before adequate measures can be taken for their destruction.

3. To prevent the access of non-immunes to localities in which contaminated mosquitoes may still be alive.

The fact that by satisfying these conditions the propagation of yellow fever can be absolutely controlled has been fully demonstrated by Major W. C. Gorgas while he was at the head of the Sanitary Department of Havana, and by our subsequent experience in the same city, showing that non-immunes run no risk of becoming infected by staying in the presence of imported cases of the disease, when both the patient and the non-immunes are effectually protected against the bites of the yellow-fever mosquito. *Charles J. Finlay.*

YELLOW FEVER: SYMPTOMATOLOGY AND TREATMENT. See The Appendix.

YELLOW SPRINGS.—Greene County, Ohio. Hotel.

Access.—Yellow Springs is a station on the Little Miami Railroad, seventy-four miles northeast of Cincinnati (Walton).

The springs are pleasantly situated on the banks of the Little Miami River. The surrounding country is undulating, and attractive drives lead in all directions. The springs yield about six hundred and sixty gallons of water per hour. An analysis by Messrs. Wayne and Locke resulted as follows: One United States gallon contains (solids): Calcium carbonate, gr. 19.57; calcium sulphate, gr. 1.35; sodium chloride, gr. 0.15; magnesium chloride, gr. 0.17; calcium chloride, gr. 1.54; iron oxide, gr. 0.39. Total, 23.17 grains.

The water possesses mild diuretic and tonic properties. *James K. Crook.*

YELLOW SULPHUR SPRINGS. — Montgomery County, Virginia.

Post-Office.—Yellow Sulphur Springs. Hotels and cottages.

Access.—Via Norfolk and Western Railroad to Christianburg depot, thence three and one-half miles by stage to springs.

This resort is located near the summit of the Alleghany Mountains, at an elevation of 2,000 feet above the sea. We find here the usual beautiful scenery and charming climate characteristic of the Alleghany resort. Four miles north of the springs is the village of Blacksburg, the location of the Virginia Agricultural and Mechanical College and the State Experimental Station. The Montgomery White Sulphur Springs are also within a distance of only four miles. The Alleghany Springs are fifteen miles, and the wonderful Mountain Lake and Bald Knob eighteen miles distant. A large new hotel, having sixty-four bed-chambers, a handsome ball-room, a large and well-ventilated dining-room, numerous bath-rooms, etc., are among the recent improvements. The lawn and pleasure grounds are shaded by magnificent forest trees, whose dense foliage makes a delightful and luxurious shelter in warm weather. The Yellow Sulphur Springs yield one hundred and eighty gallons of water per hour. This water, which has a temperature of 55° F., is transparent and very palatable. Baths of this water are always to be had at any desired temperature. The following analysis of the water is taken from the United States Dispensatory for 1880, p. 1832:

One United States gallon contains (solids): Calcium carbonate, gr. 8.64; magnesium carbonate, gr. 1.38; iron carbonate, gr. 0.62; free carbonic acid, gr. 4.68; calcium sulphate, gr. 63.30; magnesium sulphate gr. 21.09; aluminum sulphate, gr. 3.18; potassium sulphate, gr. 0.11; sodium sulphate, gr. 0.75; calcium phosphate, gr. 0.01; magnesium phosphate, gr. 0. 01; potassium chloride, gr. 0.09; sodium chloride, gr. 0.08; organic matter, gr. 3.73; and traces of iron protoxide. Total, 107.67 grains.

The title to the designation "sulphur" water is not made clear by this analysis, yet it shows a valuable combination of mineral ingredients. The water should possess antacid, diuretic, and laxative properties. It contains sufficient iron to give it a tonic influence and enough free carbonic acid to impart a pleasant sparkle and to endow it with a grateful sedative action on the stomach. The water has been found, on continued use, to brace up and give tone to the muscular system and to allay chronic and subacute inflammation of the gastro-intestinal mucous membrane, thus regulating the secretory function, tranquillizing the nervous system, and tending to promote sound and refreshing sleep. It is highly recommended in chronic disorders of the female generative organs, especially in amenorrhœa, in dysmenorrhœa of cer-

tain forms, and in leucorrhœa. It also acts as a valuable restorative in general debility and in convalescence from acute prostrating diseases. The baths are recommended for rheumatism and chronic squamous skin affections.

James K. Crook.

YELLOWSTONE NATIONAL PARK SPRINGS.—The great Yellowstone Park is undoubtedly destined to become prominent as a health resort. Within its limits are contained upward of two thousand springs, many of which have been found to be highly mineralized as well as thermal. We present the following table of reactions, etc., of thirty-four of these springs, geysers, and streams, which we have compiled from analyses made in 1883, 1884, and 1885 by Messrs. Frank Austin Gooch and James Edward Whitfield*:

SPRINGS AND GEYSERS OF THE YELLOWSTONE NATIONAL PARK.

	Temperature F.†	Reaction	Solid contents per U. S. gallon.‡
			Grains.
Cleopatra Spring	159.80	Alkaline	121.64
Orange Spring	145.40	"	101.54
Hot River	136.40	"	113.10
Soda Bath Spring	64.40	"	
Fearless Geyser	191.40	Neutral	95.02
Pearl Geyser	187.20	"	
Constant Geyser	197.60	Acid	94.15
Coral Spring	163.40	"	111.35
Echinus Spring	195.80	"	18.58
Schlangenkessel	195.80	"	98.52
Fountain Geyser	179.60	Alkaline	81.03
Great Fountain Geyser	179.60 to 199.80	"	76.37
Hygeia Spring	199.40	"	68.79
Madison Spring	140.00	"	76.95
Excelsior Spring	197.60	"	85.40
Old Faithful Geyser	189.20 to 191.40	"	81.03
Splendid Geyser	199.80	"	95.02
Giantess Geyser	199.80	"	82.20
Bee-hive Geyser	199.80	"	70.54
Grotto Geyser	199.80	"	82.58
Turban and Grand Geysers	195.80	"	81.03
Artemisia Geyser	192.02	"	86.28
Taurus Geyser	197.60	"	74.62
Asta Geyser	187.20	"	39.05
Bench Spring	191.40	Slightly acid	27.40
Chrome Spring	197.60	Neutral	196.32
Alum Creek		Acid	71.12
Mush-pot Spring	185.00	"	64.15
Devil's Ink Pot	197.60	"	197.05
Firehole River at Marshalls	44.40	Alkaline	24.36
Gardiner River above Hot River	44.40		12.24
Water Supply at Mammoth Hot Springs			15.74
Soda Springs	42.80	Acid	18.80
Yellowstone Lake			99.11

† Converted from degrees centigrade.
‡ Converted from grams per kilograms.

Most of these waters, it will be seen, are not only highly thermal, but are quite heavily mineralized, the solid contents ranging from 12.24 to 197.05 grains per gallon. These mineral ingredients consist chiefly of calcium, sodium, potassium, lithium, magnesium, silicon dioxide, sulphur trioxide, carbon dioxide, chlorine, and basic oxygen. The chemists also discovered the following ingredients in small quantities or traces: Titanium, arsenic, iron, bromine, aluminum, manganese, barium, strontium, rubidium, cæsium, ammonium, hydrogen sulphide, boron, phosphoric and hydrochloric acids. The various combinations of these elements and bases have not been fully determined, but the waters may in general terms be classed as calcic, alkaline, silicious, saline, and sulphureted. It may be stated that the waters for the above examinations were collected during the months of July, August, September, and October, and the thermometric records represent as a rule the summer temperatures. It is probable that the waters of the hot springs show little variation in temperature at the fountains during the year. We present in full the analysis of the Fountain Geyser, which may be regarded as fairly representative of the group. The hypothetical combinations have been worked out for the author by E. E. Smith, M.D., Ph.D., of New York.

Fountain Geyser (Yellowstone National Park). One United States gallon contains (solids):* Sodium chloride, gr. 30.47; potassium chloride, gr. 2.09; sodium bromide, gr. 0.03; lithium bicarbonate, gr. 1.98; sodium bicarbonate, gr. 22.46; magnesium bicarbonate, gr. 0.35; calcium bicarbonate, gr. 0.33; iron bicarbonate, gr. 0.035; potassium sulphate, gr. 2.48; sodium phosphate, gr. 0.01; sodium tetraborate, gr. 1.16; sodium arseniate, gr. 0.20; alumina, gr. 0.96; silica, gr. 19.33; and a trace of manganese bicarbonate. Total, 81.885 grains. The water also contains free carbonic acid and a trace of sulphuretted hydrogen.

This analysis presents a fairly strong alkaline-saline water. It possesses useful properties as an antacid, diuretic, and aperient. In addition, it contains an appreciable quantity of arsenic, and in continued dosage should speedily produce the physiological effects of that drug. The water of La Bourboule, in France, which contains but slightly more arsenic than this geyser, has long been celebrated in the treatment of skin diseases, notably in eczema and the other rheumides. The Yellowstone waters will no doubt in time be found to possess equal virtue in these affections. At the present time the waters are used for bathing only at the Fountain Geyser Hotel. At this resort the waters are conducted into the hotel building, which is supplied with an excellent system of bath-rooms. The thermal waters of the park will probably come into high repute, in the near future, in the treatment of gout, rheumatism, and syphilitic affections. Some of the springs contain a considerable proportion of sulphureted hydrogen, while free hydrochloric acid is found in several others. We may expect that all of these different waters will at some future time render useful service in practical therapeutics. We are informed that intensely hot weather is practically unknown in the park. Following is a temperature table of the summer and early autumn months, made during a recent season:

	Sunrise.	Midday.	Sunset.	Mean.
July	55° F.	77° F.	69° F.	67° F.
August	50	70	60	65
September	41	66	58	55
October	41	57	52	50

Visitors to the park should be amply prepared for cool weather, no matter what the season may be.

James K. Crook.

YERBA SANTA.—(*Eriodictyon*, U. S. P.; "Consumptive's weed," "Mountain balm," etc.) The dried leaves of *Eriodictyon Californicum* (H. et A.) Greene (fam. *Hydrophyllaceæ*). A very pretty evergreen shrub, growing on the western side of the United States and in northern Mexico, in gregarious clumps and patches in barren soils and among rocks. The drug is thus described: Usually much broken; blade narrowed into a very short and broad petiole, 5–12 cm. (2–5 in.) long and rarely exceeding 3 cm. (1¼ in.) in breadth, oblong-lanceolate, gradually tapering to an acutish point, most irregularly serrate- or crenate-dentate, thick and brittle, or flexible in a damp and warm atmosphere, the margins more or less incurved; upper surface yellowish-green, more or less resinous, smooth, the veins somewhat impressed; lower surface whitish or yellowish-white, with finely and conspicuously reticulate dark veins, densely but very shortly tomentose; odor somewhat aromatic, strongly balsamic if heated in the closed hand; taste balsamic, sweetish, somewhat tea-like.

The principal constituent of this drug is its ten to

* Bulletin 47 of the United States Geological Survey, 1888.

* The combinations, as estimated by the original analysts, have recently come under our observation. The result does not materially differ from those given above. It is probable that the proportion of sodium arseniate is somewhat over-estimated.

twelve per cent of resin, divisible into two parts, one of which, constituting its chief bulk, possesses the property of precipitating quinine from its salts. It also contains volatile oil, cericinol sugar, and the peculiar body *eriodictyonic acid*, which in some respects resembles tannin.

Yerba santa, as one of its names shows, has a local reputation on the Pacific slope for coughs, colds, bronchitis, and phthisis, a reputation which is shared by many other resinous substances and has some foundation. It is also a pretty good vehicle for the administration of quinine, whose taste, like liquorice or glycyrrhizin, it covers pretty well. Of the official fluid extract, 3 or 4 c.c. (♏ xlv. ad lxv.) may be given for coughs. A syrup, as a vehicle for quinine, is sometimes prepared.

Henry H. Rusby.

YOLK SAC.—(Umbilical vesicle: Vitelline sac.) Since the human yolk sac is a vestigial organ, its significance can be appreciated only after examining the corresponding structure in other animals.

Comparative Embryology.—In fish embryos the entoderm lining the digestive tract is distended ventrally, and its cells are loaded with nutritive material in the form of granules. This solid mass of yolk-laden entoderm is covered on the outside with a layer of mesoderm, and the entire structure is known as the yolk sac. In sharks the sac joins the body by a constricted portion, the yolk stalk (Fig. 5046, *A*). The ventral body wall, composed of ectoderm with a lining of mesoderm, extends over the yolk sac, but is separated from it by an extension of the body cavity or cœlom. As the fish grows, the yolk is consumed as food and the ventral swelling is gradually taken up until no trace of it remains. In the mesoderm of the yolk sac blood-vessels develop very early and extend to and from the body of the embryo. In some viviparous sharks the vascular yolk sac is thrown into folds which, by fitting into corresponding uterine folds, also vascular, constitute a sort of placenta (Balfour).

In birds the yolk material is enormously developed, and, though not at first divided into cells, is still to be regarded as intracellular and as belonging chiefly to the entoderm. The germ layers spread gradually over its surface (Fig. 5046, *B*). The small embryo sinks into the yolk mass, and the ectodermal layer, with the accompanying mesoderm, closes in over its back to form the amnion, *Am*, and to become cut off from the chorion, *Cho*. The extra-embryonic cœlom consequently becomes dilated. These relations are further illustrated in the cross section, Fig. 5047. From the posterior end of the intestinal tract an out-pocketing projects into the cœlom, in which it lies free. This entodermal pocket is the allantois, an organ composed of the same layers as the yolk sac, and like it, highly vascular. Its competition with the yolk sac in placental mammals will be described presently. The yolk sac of birds, in later stages, is drawn into the abdominal cavity, and there it remains in water fowl, as a permanent diverticulum at about the middle of the small intestine. (Oppel.)

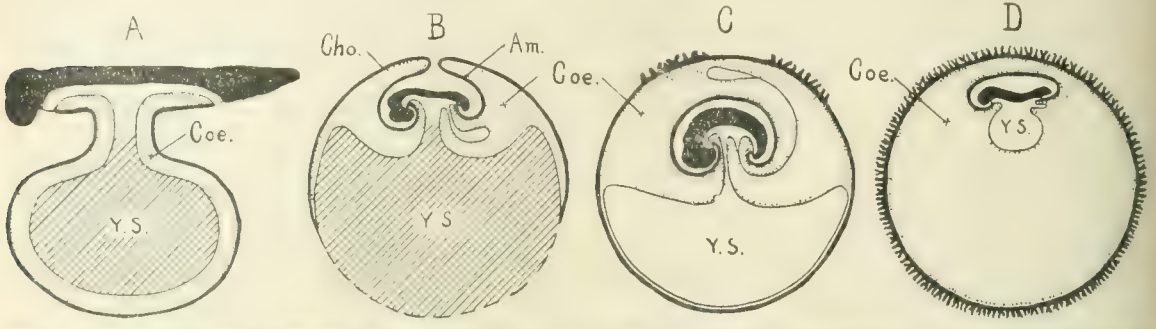

Fig. 5046. Diagrams illustrating the Development of the Yolk Sac: *A*, in fish; *B*, in birds; *C*, in the rabbit; *D*, in man. The embryos are drawn in black, the ectoderm in heavy lines, the entoderm in light lines, and the mesoderm in dotted lines. The yolk is shaded. *Am.*, Amnion; *Cho.*, chorion; *Coe.*, extra-embryonic cœlom; *Y. S.*, yolk sac. (After Hertwig, Duval, and Minot.)

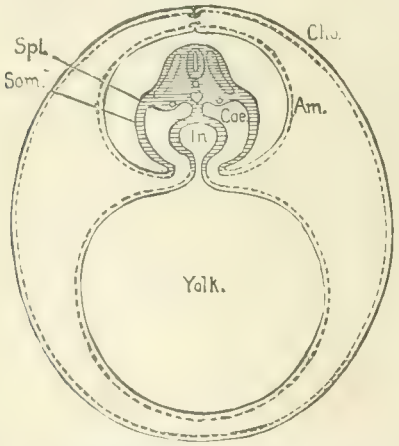

Fig. 5047.—Diagrammatic Cross-Section of an Amniote Embryo. The body of the embryo is shaded; the extra-embryonic mesoderm is represented by a dotted line. *Som*, somatopleure; *Spl*, splanchnopleure; *Cho*, chorion; *Am*, amnion; *Coe*, cœlom; *In*, intestine; *Yolk*, yolk sac. (Minot.)

The mammals present several types of yolk sac. Except in the monotremes the sacs are empty; the yolk-charged protoplasm has given place to a single layer of well-defined entodermal cells surrounding a cavity filled with thin fluid. The conditions in the rabbit, at a stage comparable with the bird, *B*, are shown in Fig. 5046, *C*. The allantois does not lie free in the cœlom, but has fused with the chorion, into which its vessels extend to form the fœtal part of the placenta. In the rabbit the cœlom never extends farther around the yolk sac than is shown in the figure. The lower half of the sac consists of entoderm and ectoderm only. This lower half soon breaks down and disappears, leaving the entoderm of the upper half to rest against the uterine wall. It is then said to become villous and perform placental functions. (O. Schultze.) Except in some rodents and in the marsupials, the mesoderm extends completely around the yolk sac. In the marsupials the sac is large, almost enveloping the embryo and its amnion. It unites with the chorion and becomes the fœtal portion of the placenta. (Osborn.) The allantois in these animals does not reach the chorion. In the carnivora both yolk sac and allantois are connected with the chorion until birth, and both are vascular. The horse shows similar relations, but the area of chorionic connection with the yolk sac becomes very small, and at birth is merely a scar. (Bonnet.) In ruminants and swine the contact of sac and chorion is slight and transient. In Tarsius and the primates the yolk sac is very small, and in early stages quite distant from the chorion (Fig. 5046, *D*). The extra-embryonic cœlom is correspondingly greatly developed. The human

yolk sac is therefore a small and rudimentary organ, neither containing yolk material nor performing placental functions.

Gross Anatomy of the Human Yolk Sac.—The youngest human embryos known, and those 1.5 mm. long, are attached to a rounded yolk sac having a diameter equal to the length of the embryo and being connected with nearly the whole extent of the intestinal tract. The embryo grows faster than the yolk sac. At 2.15 mm. the relations are those shown in Fig. 4827 in the present volume. The opening of the globular yolk sac now occupies the middle third of the entodermal tract. A little later the sac becomes pyriform (Fig. 4829), and its intestinal orifice is relatively much smaller. In embryos of about 7 mm., or in the fourth week, the yolk sac is said to attain its maximum development. It is then round or oval, 4–7 mm. in diameter, connected with the intestine by a slender yolk stalk. The sac lies between the amnion and the chorion; its stalk has become included in the umbilical cord (see *Umbilical Cord*, and Fig. 4831). Subsequently the yolk stalk loses its lumen and proceeds to disintegrate, beginning at a point near the future umbilicus. Thus in a three months' embryo the yolk stalk is found in the proximal part of the cord, but no trace of it exists in the distal portion. At birth the part within the cord has gone, but beyond the cord, between the chorion and amnion, traces of it are found, and the sac itself is almost invariably present. (? Mayer, 1834; B. S. Schultze, 1861.)

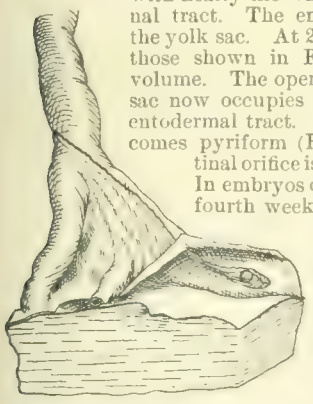

Fig. 5048. The Placental Insertion of an Umbilical Cord, showing Schultze's Fold. A part of the amnion covering the fold has been reflected, disclosing the yolk sac and persistent vitelline vessels. One-half natural size. (After Lönnberg.)

The umbilical cord is attached to the mature placenta at an angle varying from 0° to 90°. If the cord is gently extended, a thin, triangular or crescentic fold may be expected in this acute angle of insertion. It is thinner than other folds, which are due to blood-vessels. Sometimes it is inconspicuous or absent; in other cases it is 5 or 6 cm. high and very prominent as in Fig. 5048. It is the only place where the amnion is not closely adherent to the cord. In it and beyond it Wharton's jelly is found, sometimes extending a considerable distance over the placental surface. The amniotic villi occur chiefly on this fold. (Winkler, 1868.) According to its discoverer, Schultze, the fold is caused by the yolk stalk, which, if present, is seen within it as a delicate thread running just beneath the surface. It may be absent, or present in detached fragments; occasionally it is continuous from the cord to the yolk sac. If the amnion is removed from the chorion in the quadrant indicated by Schultze's fold, the *sac* will appear as a round or oval vesicle adhering to the amnion (rarely to the chorion), being about 5 mm. in diameter, and possessing a whitish, yellow, brown, or greenish nucleus. Lönnberg, in two hundred placentas, found the yolk sac under the placental area thirty-one times, at the placental border nine times, and beyond the placenta one hundred and sixty times, an extreme case being 27 cm. from the placental insertion of the cord.

The proximal end of the yolk stalk enters the ileum. In young embryos the extensive loop of intestine to which the stalk is attached is found outside of the body, in the cœlom of the umbilical cord. As the intestine is withdrawn into the body, a part of the yolk stalk passes from the navel inward, to a point on the small intestine which at birth is about one foot from the cæcum, and in the adult some four feet. This section of the yolk stalk is normally obliterated. The place where it entered the intestine may be marked by a diverticulum, generally less than four inches in length, although sometimes much longer, known as Meckel's diverticulum. Meckel in 1809 understood its origin and knew that the yolk sac was never connected with the vermiform appendix!

Blood-vessels. — The vitelline, omphalo-mesenteric, or omphalo-mesaraic vessels, which supply the yolk sac, are among the first blood-vessels to develop. In young chick embryos blood from the yolk sac enters the body by two veins which unite to form the heart. These are the vitelline veins. From the heart two arteries extend back along the body of the embryo and branch out on either side over the yolk sac. There a vascular network places them in connection with the veins just described. In later stages a caudad continuation of each artery in the body of the chick causes the portion which passes to the yolk sac to appear as a branch, the vitelline artery. The stems from which these branches arise fuse to form the dorsal aorta. In mammals there are at first many vitelline arteries on each side, irregularly distributed. These are replaced by a few vessels said to be segmentally arranged in pairs. (Mall, Tandler.) Finally a single pair becomes predominant.

By the early development of the vitelline circulation the nutritive yolk is transferred to the body. The spread of the vascular network over the yolk proceeds from the embryonic pole. Its extent is bounded by an encircling vessel, the terminal sinus. This sinus is well defined in birds, is less distinct in mammals, and in man has never been seen, since in the youngest known human embryos the yolk sac is already completely covered with blood-vessels. In birds the vitelline area is the seat of the extensive formation of blood corpuscles, and in mammals it may have the same function.

The vitelline arteries fuse with one another between the aorta and the intestine, and again ventral to the intestine. The intestine becomes encircled by a vascular ring, one half of which, usually the left, soon disappears. A single vitelline artery is thus formed which passes on the right side of the intestine to the yolk sac. With the degeneration of the yolk sac this artery is obliterated, except that portion between the aorta and intestine, which remains as the superior mesenteric artery.

The vitelline veins, at first a pair, also fuse, and form two loops around the intestine. From the intestine they extend as a single fused vessel across the abdominal cavity to the umbilicus. The distal part of this vein is later obliterated. Portions of the loops around the intestine become the portal vein, from which a new branch arises to form the superior mesenteric vein (Dexter).

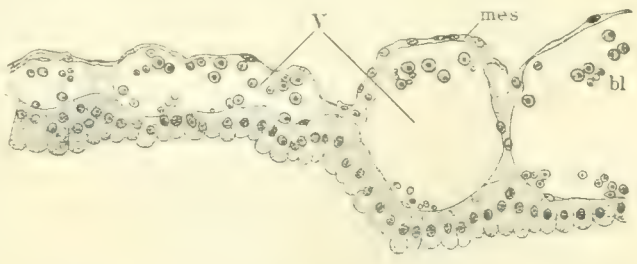

Fig. 5049.—Vertical Section of the Wall of the Yolk Sac of a Rabbit Embryo of Thirteen Days. V, Blood-vessels; *bl*, blood-cells; *mes*, mesoderm. (Minot.)

In the carnivora the vitelline vessels are pervious for a few days after birth In man the extra-abdominal part is usually obliterated in the first half of pregnancy. Cases of persistent vitelline vessels at birth have been reported, first by Bischoff in 1834. Lönnberg states that there may be two, three, or four vessels, usually three. The arteries may anastomose with the umbilical arteries, but the vein goes through the cord to enter the fœtus

directly. Fig. 5048 shows the persistent vessels around the yolk sac.

Histology.—The wall of the yolk sac of a young rabbit consists of two layers, a lining of simple cylindrical entodermal epithelium and an outer layer of vascular mesoderm (Fig. 5049, from Minot). The latter soon appears divisible into mesenchyma and mesothelium. These with the entoderm make the three layers which are characteristic of later stages. The lining of the human yolk

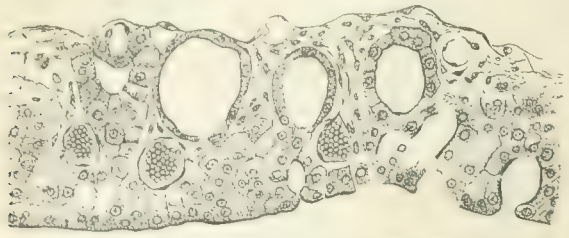

Fig. 5050. Cross Section of a Human Yolk Sac, from a 9.4 mm. Embryo. 95 diameters.

sac is said to be of simple epithelium at first. Subsequently it becomes stratified and thrown into folds, variously interpreted. Kölliker and von Baer have described villi containing blood-vessels, and Paladino has figured irregular elevations in the yolk sacs of dog and rabbit. Tourneux found epithelial depressions extending into the mesoderm, separated from one another by mesodermal papillæ. Spee observed slender tubes of entoderm extending across the mesoderm, branching dichotomously, and ending in alveolar enlargements. These he found all over human yolk sacs of six to nine weeks. With Paladino, who regards the mammalian yolk sac as a gland with an internal secretion, and Saxer who finds it a blood-forming organ containing giant cells and blasts, Spee unites in making comparisons with the liver.

The yolk sac of a human embryo 9.4 mm. long, of about four weeks, is without villi. Its proliferated epithelium shows alveolar pockets sometimes resting on the mesothelium and often having no outlets. Between the alveoli there is a small amount of vascular mesoderm, covered with a layer of mesothelium (Fig. 5050).

In a better preserved yolk sac from a 23 mm. embryo of about two months, only an occasional epithelial cyst is found. The dense mesenchyma forms a more definite layer, and the mesothelium is quite distinct (Fig. 5051). The blood-vessels cause elevations on the outer surface which are macroscopic. The entodermal cells are vacuolated, probably containing fat droplets, and are degenerating. They possibly account for some of the stages in blood formation described by Saxer. The resemblance with the liver seems to be remote. At birth the entoderm has wholly disappeared, leaving a connective-tissue

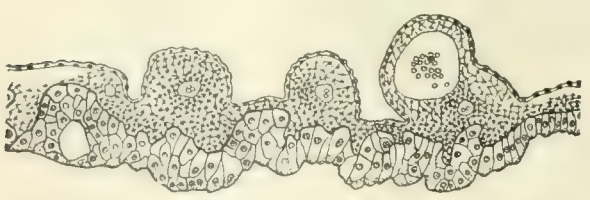

Fig. 5051. Cross Section of a Human Yolk Sac from a 23 mm. Embryo. 95 diameters.

envelope surrounding débris, calcareous granules, fat, and albuminoid bodies (Lönnberg). Rauber described yolk elements lying free in the mammalian yolk sac. If yolk is present it should be within the entodermal cells; probably Rauber's yolk is a degeneration product.

The yolk stalk in the cord can be distinguished from the allantois by its cylindrical epithelium, generally simple, but sometimes two- or three-layered. The epithelium of the allantoic duct is cuboidal.

Pathology.—Meckel's diverticulum may contain concretions, and become inflamed like the vermiform appendix. The intra-abdominal yolk stalk sometimes persists as a band of fibrous tissue, a frequent cause of intestinal obstruction. (Fitz.) Portions of the stalk may form large cysts, and be connected with the intestine or the umbilicus, or lie free in the mesentery. (Roth.) The stalk may remain open from intestine to umbilicus, producing an intestinal fistula. (Neurath and Roth.) Fungiform adenoma at the umbilicus has been attributed to the yolk stalk remains. (Hüttenbrenner.) Cysts which may be numerous along the extra-abdominal yolk stalk (Ahlfeld) and persistent vitelline vessels have no harmful effect upon the fœtus.

Frederic Thomas Lewis.

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YOUNG'S NATURAL GAS WELL AND MINERAL SPRINGS.—Lake County, California.

These natural wonders are located in the eastern edge of Kelseyville on a slightly elevated ground, about three miles south of Clear Lake and near the base of Uncle Sam Mountain. The well is, so far, more of a curiosity than a health resort. While boring for gas, in 1888, the proprietors set free, at a depth of about one hundred and fifty-eight feet, a large volume of water mingled with gas. It rushed out with great force, and the flow has continued, geyser fashion, ever since. For an instant it stops, and then comes another violent ejection to the height of about forty feet; this occurs as often as seventy or eighty times to the minute. The flow of water, which has a temperature of 76° F., is about six thousand gallons per hour. Many people from various localities visit the place to witness the peculiar phenomenon. The water has been extensively used by the people of Kelseyville and vicinity, and they pronounce it excellent for liver, kidney, and bowel disorders. The following analysis of the water was made by Winslow Anderson in 1889. One United States gallon contains (solids): Sodium chloride, gr. 15.76; sodium carbonate, gr. 36.52; sodium sulphate, gr. 19.16; potassium carbonate, gr. 3.40; potassium iodide, gr. 0.78; magnesium carbonate, gr. 7.14; magnesium sulphate, gr. 21.90; calcium carbonate, gr. 6.36; calcium sulphate, gr. 9.72; manganese carbonate, gr. 0.18; ferrous carbonate, gr. 4.95; borates, gr. 3.12; alumina, gr. 5.18; silicates, gr. 6.45; and traces of barium carbonate, lithium carbonate, and organic matter. Total solids. 140.62 grains. Free carbonic acid gas, 9.60 cubic inches; also traces of petroleum and carbureted hydrogen (inflammable gas).

The water may be described as a fairly strong saline chalybeate. If sufficiently palatable it ought to prove useful as a therapeutic agent. Its action is tonic, antacid, aperient, and diuretic. It is the owner's intention to establish a health and pleasure resort on the premises. Several inflammable gas wells are also found on the ground. These yield a gas composed largely of light carbureted hydrogen. *James K. Crook.*

YUMA, ARIZONA.—This desert "city" of 1,800 inhabitants lies in the extreme southwestern corner of Arizona, at the junction of the Gila and Colorado rivers. It has an elevation of only 140 feet, and is situated in the Great Arizona Desert, about sixty miles from the Gulf of California and a few miles from the Mexican border. It is on the line of the Southern Pacific Railroad.

Like Phœnix in the same State, Yuma is famed for its sunshine, heat, and dryness. It can be used only as a winter resort, for it is excessively hot in the summer, the thermometer sometimes rising as high as 115° F. or over, and for many days in succession it ranges above 90° F.

Such a region and climate present conditions closely resembling those which are found at the health resorts of Egypt, which are in nearly the same latitude. The accommodations in the latter country, however, are vastly superior in abundance and excellence to those at Yuma, which are insignificant in comparison, although we are told that "ample accommodation is had at the Depot Eating House, situated on the very bank of the Colorado, with encircling balconies for enjoyment of guests." One would hardly choose, however, a railroad station for a pulmonary invalid seeking pure air free from dust. What other suitable accommodations, if any, exist is unknown to the writer. There is little at Yuma to attract one in the way of amusements or diversion. Such vegetation as is found here is of a semitropical nature. The soil is that which is peculiar to all desert regions.

The climate is that typical of the desert in a tropical latitude, and presents many interesting phases for study. In the first place, we observe from the chart that there are 282.4 clear days, and 351.7 clear and fair days, or over 90 per cent. The mean number of cloudy days for 6 years was 21 (Solly). One may therefore enjoy here almost continuous sunshine. What a contrast, for instance, to Sitka, Alaska, where there are only 66 clear days on an average during the year! Secondly, the extraordinary heat of the warmer months of the year is to be noticed, the temperature in the shade having been known to rise as high as 118° F.; and in the year 1893, from April to October inclusive, out of 214 days, there were 162 during which the thermometer stood above 90° F., and the maximum temperature for the year was 111° F. (Solly, "Medical Climatology.")

It is to be borne in mind, however, that this is a very dry heat—the dryness of the desert, and hence more endurable than a lower temperature would be in combination with a moist atmosphere. From the table we see, again, that the relative humidity is very low, 40.3 per cent. for the year; and the average rainfall for the year only 2.08 inches, and in some years much less than his. Thus, for example, in 1899, there was only 0.6 inch of rain, 0.5 of which fell in November. (Hinsdale, "System of Physiologic Therapeutics, Climatology.") The winter climate, the season in which an invalid would seek such a resort, is sunny and mild, the average temperature being 56.1° F., about five degrees higher than that at Phœnix for the same season, and about two degrees lower than that of Cairo, which is 58.3° F.

Climate of Yuma, Arizona. Latitude, 32° 45'; Longitude, 114° 36'.—Period of Observation, Eight Years.

	Jan.	Feb.	March.	May.	July.	August.	Oct.	Nov.	Dec.	Year.
Temperature—Degrees Fahr.										
Average or normal	53.5	59.0°	65.0°	[illegible]	92.4°	91.0°	72.0°	60.5°	56.0°	72.1°
Mean of warmest	60.3	65.0	71.8	[illegible]	94.0	92.7	77.0	65.4	59.3	74.0
Mean of coldest	50.2	52.2	58.3	74.4	89.6	88.6	66.7	56.7	52.8	70.2
Average daily range	10.1	12.8	13.5	7.4	4.4	4.1	10.3	8.7	6.5	3.8
Highest or maximum	80.0	90.0	100.0	108.7	118.0	115.0	102.0	91.0	80.0	
Lowest or minimum	22.5	25.0	31.0	49.0	61.0	64.0	41.4	31.0	27.0	
Humidity										
Average relative	44.6%	42.2%	41.0%	[illegible]	[illegible]	42.5%	40.1%	38.9%	44.6%	40.3%
Precipitation—										
Average in inches	.43	.52	.08	.01	.22	.25	.04	.03	.31	2.08
Wind—										
Prevailing direction—From	N.	N.	W.	W.	S.	S. E.	N.	N.	N.	N.
Average hourly velocity in miles	5.6	7.0	5.9	5.8	6.0	5.5	4.4	5.2	4.9	5.5
Weather—										
Average number clear days	20.8	19.2	23.1	28.0	22.5	21.8	24.1	22.8	22.4	282.4
Average number fair days	8.1	6.6	6.6	2.6	7.8	7.7	6.1	5.8	6.9	66.3
Average number clear and fair days	28.9	25.8	29.7	30.6	30.3	29.5	30.2	28.6	29.3	351.7

For a comparison of the climate of this desert region of Arizona with that of the winter resorts of Egypt, the reader is referred to the article on the latter country in Vol. III. of this Handbook. It will be seen how closely the climatic characteristics of these two regions resemble each other; both illustrate the features of a warm desert climate, and with equally good accommodations and attractions both would probably produce similar results in the treatment of disease.

The conditions and diseases for which such a climate as that to be found at Yuma is to be recommended are also those for which the Egyptian climate is favorable. All stages of phthisis may be favorably influenced by a residence in this desert climate, provided the conditions are not acute. As in Egypt, the disadvantage of such a resort is the short time of year during which it is available; this is a distinct objection in the treatment of phthisis, although even with this disease change is sometimes desirable and advantageous, and this is oftener true of many other maladies. Change *per se* is a therapeutic resource of no mean value.

For the consideration of the climate of Arizona as a whole, the reader is referred to the article on *Arizona* in Vol. I. of this Handbook. *Edward O. Otis.*

ZEA. See *Corn Silk.*

ZEDOARY.—(*Rhizoma Zedoariæ*, P. G.) The rhizome of *Curcuma Zedoaria* Roscoe, order *Zingiberaceæ*. This is one of the numerous ginger-like plants which inhabit the warmer parts of Asia, and whose rhizomes or seeds are used as spices or condiments. Zedoary is indigenous in India and China, in which places it is also cultivated. It is introduced and cultivated also in Java and other Pacific islands. The rhizome is the part used, being dug up, washed, or scraped, and then sliced and dried. It is commonly stated that the smaller branches form the "long Zedoary," and the central tubercles or clumps the "round Zedoary"; but, according to the French Codex and some other authorities, the latter is the rhizome of a related plant, *C. aromatica* Salisbury. Zedoary comes

also occasionally mixed with curcuma. The long variety of Zedoary is of old occurrence in commerce, and was formerly a greater favorite than now, when its place is mostly taken by ginger, curcuma, sweet flag, etc. In this country, indeed, it is wellnigh obsolete, but on the continent of Europe it is still official in most countries, although but very little used.

It figures mostly in external applications as an ingredient of several proprietary liniments and "balsams." The French "*Baume de Fioraventi*" contains zedoary along with fifteen other resins and spices.

In its composition zedoary resembles ginger and curcuma, and like these it contains an abundance of starch.

W. P. Bolles.

ZEM ZEM SPRINGS.—Lake County, California.

These springs are located on the southeastern side of Clear Lake, and take their name from the Holy Well in Mecca. The waters have a temperature of 64° F., and, according to an analysis said to have been made by Dr. Boon, they contain the following ingredients: One United States gallon contains: Sulphur, gr. 291.15; iron, gr. 157.50; magnesia, gr. 163.24; solid matter, gr. 612.15. Total solids, 1,224.04 grains.

They have some notoriety in the treatment of dyspepsia, rheumatism, and diseases of the liver and kidneys.

James K. Crook.

ZENKER'S NECROSIS. See *Muscle, Pathology of*, and *Necrosis*.

ZINC.—I. General Medicinal Properties of Compounds of Zinc.—Charging the blood with zinc affects nutrition in excess, developing poisonous symptoms, but the action is not so profound as with the majority of the heavy metals, and in medicinal dosage deleterious effects need not be feared. Therapeutically, the constitutional influence shows itself in a tendency—not very strongly pronounced, but still useful—to abate spasmodic nervous disorders, such as epilepsy, chorea, hysteria, etc. Indeed, before the rise of bromides into medicinal prominence, zinc was a standard medicine for the relief of epilepsy and hysteria. At present, it can only be said that, among the heavy metals, zinc combines more potency and availability as a constitutional nervine than any other—which is not saying much. Locally, the properties of the zinc compounds differ with the chemistry of the different compounds, mainly according to solubility, the soluble salts being caustic or irritant and astringent, and the insoluble compounds operating as absorbent, soothing, healing, and disinfectant dressings. Internally, the soluble compounds in moderate dosage determine prompt and thorough vomiting, after the manner of copper salts, though with less severity of action. In large doses they are corrosive or irritant poisons, according to the activity of the individual compound. The insoluble compounds in small dose allay gastric and intestinal irritability, but in large dose, probably through chemical conversion, may nauseate, and even vomit. Zinc compounds are disinfectant, the soluble salts, especially the chloride, notably so, and since they do not stain they are the most generally available of metallic salts for the purpose.

The *therapeutics* of zinc consist of the following applications: *constitutionally*, as a medicine of second- or third-rate power to control spasmodic nervous disease; *in the stomach*, to allay pain or nausea, for which purpose an insoluble compound is commonly selected; *in the bowels*, to control diarrhœa, especially when the affection seems a reflex of nervous irritation rather than the expression of a catarrh; and, *externally*, the soluble compounds, to cauterize, or, to perform the usual functions of a metallic astringent irritant in the way of determining absorption of granulation tissue, and abating catarrh; and the insoluble preparations to act as soothing, healing, or, applied dry, absorbent and disinfectant dressings. Solutions of the soluble salts are also available as efficient disinfectants of their kind for wounds, fabrics, floors, and all non-metallic receptacles.

II. The Compounds of Zinc Used in Medicine.—These are the *oxide, carbonate, chloride, bromide, iodide, sulphate, acetate, valerianate*, and *phosphide*, and although not official, the *nitrate* and *oleate*.

Zinc Oxide (ZnO).—Zinc oxide is official in the United States Pharmacopœia as *Zinci Oxidum*, Zinc Oxide. It is a smooth white powder, odorless and tasteless, and insoluble in either water or alcohol. It dissolves in acids without effervescence. It is permanent in the air, but should be kept in well-stoppered bottles. Zinc oxide is a commercial article, and impure and even fraudulent specimens are not uncommon. Zinc oxide is the principal insoluble zinc compound. It may be used, given internally, for the constitutional effect of zinc, or to allay vomiting or diarrhœa; dose, from 0.06 to 0.30 gm. (gr. i.–v.), several times a day, in powder or pill. Externally, zinc oxide may be used, alone or mixed with powdered starches or gums, as an absorbent powder dressing to excoriations and sores, or, in ointment, as a soothing and healing application, for which purpose it is very efficient. There is an official ointment, *Unguentum Zinci Oxidi*, Ointment of Zinc Oxide, consisting of twenty per cent. of the oxide in benzoinated lard, which may be applied in full strength to sores or eruptions.

Zinc Carbonate.—Normal zinc carbonate occurs in the mineral *zinc spar* or *calamine*, which was formerly official in the United States Pharmacopœia, as a medicine, but was dropped, because of its impurities, in the revision of the Pharmacopœia of 1860. In its place is official, now, the mixture of carbonates that results from precipitating a boiling solution of zinc sulphate by sodium carbonate. Such precipitate is entitled *Zinci Carbonas Præcipitatus*, Precipitated Zinc Carbonate. Precipitated zinc carbonate is, like the oxide, a smooth, white powder, without odor or taste, and insoluble in water or alcohol. It dissolves in acids with copious effervescence. Zinc carbonate is substantially a duplicate of the oxide in medicinal properties, but its use is commonly confined to external application as an absorbent powder.

Zinc Chloride ($ZnCl_2$).—The salt, commonly called *butter of zinc*, is official in the United States Pharmacopœia as *Zinci Chloridum*, Zinc Chloride. It occurs in a white crystalline powder, or in white, opaque lumps, and is exceedingly deliquescent. It is odorless, but has a very caustic saline and metallic taste (but it is so corrosive that tasting is dangerous). It dissolves very freely in water and in alcohol. It should be kept in small, glass-stoppered bottles. The chloride is the most active of the zinc salts, being highly corrosive and antiseptic both. It has little effect on the sound skin, but upon a raw surface or mucous membrane it disorganizes tissues, forming a white, tough slough. The action, though powerful, is not diffuse, so that it can be regulated quite exactly in area and depth. The slough remains odorless during its attachment, and, when finally cast off, as happens in a week or ten days, exposes an underlying surface presenting clear, healthy granulations, which rapidly proceed to cicatrization. Zinc chloride thus makes an excellent escharotic, combining the features of being powerful, yet manageable, of disinfecting its own slough for determining kindly healing of the resulting ulcer, and of being free from danger of producing constitutional poisoning. Its operation is, however, very painful. In solution, zinc chloride is a standard disinfectant, but, if strong, acts upon metallic surfaces. Internally, it is a corrosive or irritant poison, according to concentration.

For use as a caustic, patent lint may be soaked in a concentrated solution of the salt, dried, and then cut—with an old, worthless pair of scissors—into proper size and applied to the part, which, if covered with skin, must first have the epithelium removed by blistering. Much more convenient, however, is the plan of making the chloride into a paste with flour and water. Such paste can be applied moist, or may be dried and cut into pointed rods, which are then available for thrusting into any large mass requiring destruction, such as a cancerous tumor. This paste was devised by a Dr. Canquoin, of Paris, and often goes by his name. It is made by rapid

admixture of zinc chloride and wheat flour with a very little water—a few drops only to the ounce of paste. The strength in zinc salt will range from fifteen to thirty per cent., according to the character of the tissue requiring destruction.

As a disinfectant, zinc chloride can be prescribed in the official *Liquor Zinci Chloridi*, Solution of Zinc Chloride. This is a solution of the salt in water, fifty per cent., by weight, in strength. It is made directly from the metal by the action of hydrochloric acid, the resulting solution being purified from contaminating iron by a special procedure, and brought to standard strength by distilled water. The solution is a clear, colorless liquid, odorless, having a very astringent, sweetish taste and an acid reaction. In its pharmacopœial strength, this solution is entirely too strong for direct application, being, indeed, corrosive. As a general disinfectant, it should be diluted to three-per-cent. strength, and as a lotion for wound surfaces or ulcers to one per cent. It has the merit of being deodorant and disinfectant, while at the same time it has no smell, does not stain, and, in the dilution enjoined, does not attack fabrics nor injure metallic receptacles.

Zinc Bromide ($ZnBr_2$).—Zinc bromide is official in the United States Pharmacopœia as *Zinci Bromidum*, Zinc Bromide. It is a white, or nearly white, granular powder, very deliquescent, odorless, having a sharp saline and metallic taste, and a neutral reaction. It is very soluble in water and in alcohol. Because of its ready deliquescence, the salt should be kept in small glass-stoppered bottles. Zinc bromide closely resembles the chloride in general properties, being deliquescent and highly irritant. Its official recognition is, however, not for its duplicature of the chloride in uses, but for its internal employment in nervous disease, with the notion of getting the combined antispasmodic effect of zinc and a bromide. But in the small dosage which the character of salt enjoins, the quantity of bromine ingested is medicinally insignificant. The salt is given in doses of from 0.10 to 0.30 gm. (gr. iss. to v.) in syrupy solution.

Zinc Iodide (ZnI_2).—Zinc iodide is official in the United States Pharmacopœia as *Zinci Iodidum*, Zinc Iodide. This is, again, a white, granular and very deliquescent powder, odorless, but of a sharp, saline, and metallic taste. It is very soluble in water and in alcohol. It must be kept in small glass-stoppered bottles. Zinc iodide, like the bromide, resembles the chloride in quality; but, like the bromide, is suggested for the purpose of getting the effects of the acid radical along with those of zinc, in constitutional medication. But, again, the necessarily small dosage defeats the purpose. The salt is given in doses of from 0.10 to 0.30 gm. (gr. iss. to v.) in syrup. Locally, the iodide has been applied for the general purposes of the metallic astringents, in solutions ranging in strength from the one-fifth of one per cent. to six per cent., or in a twelve-per-cent. ointment.

Zinc Sulphate ($ZnSO_4.7H_2O$).—Zinc sulphate is official in the United States Pharmacopœia as *Zinci Sulphas*, Zinc Sulphate. It is crystalline, occurring in small, colorless, right rhombic prisms, or acicular needles which slowly effloresce in dry air. It is odorless, but has a sharply saline, metallic, and nauseous taste. It dissolves in 0.6 part of cold water and in 0.2 part of boiling water. It is insoluble in alcohol. It should be kept in well-stoppered bottles. Zinc sulphate is the sulphate whose commercial impure variety is called *white vitriol*. The pure quality, official as above, is in the small crystals described, which look not unlike those of Epsom salt. Zinc sulphate is decomposed by alkalies and their carbonates, hydrosulphates, lime water, soluble lead salts, and vegetable astringents. By heating, it can be made to part with its water of crystallization, forming what is called *dried zinc sulphate*.

Zinc sulphate is an irritant astringent, and, in the dried form, is even caustic, though less powerfully so than the chloride. Internally, in moderate dose, it is emetic; in excessive quantity, an irritant poison, though again less potent than the chloride. The salt is a favorite metallic astringent, being milder than copper or silver salts, of less harsh taste, and does not stain. It has thus a wide range of applicability, but yet, where a powerful action is wanted, it is distinctly inferior to silver nitrate or copper sulphate. The crystals are too small to permit the salt to be used in solid form; it is therefore used locally in solution, the strength ranging from the one-fifth of one per cent. to about four per cent. Dried zinc sulphate has been employed as a caustic, made into paste, with one-eighth part of glycerin, or into ointment with one-fourth part of lard. Internally, the salt—crystalline form—may be given for the constitutional effects of zinc, in doses of from 0.015 to 0.06 gm. (gr. ¼ to i.), several times a day; or as an emetic in doses of from 1 to 2 gm. (gr. xv. to xxx.).

Zinc Acetate ($Zn[C_2H_3O_2]_2$, $3H_2O$).—Zinc acetate is official in the United States Pharmacopœia as *Zinci Acetas*, Zinc Acetate. It occurs in soft, white, pearly, six-sided tablets and scales, which effloresce somewhat in dry air. It has a faint, acetous odor and a sharp, metallic taste. It dissolves in 2.7 parts of cold water and in 1.5 parts of boiling water; in 36 parts of cold alcohol and in about 3 parts of boiling alcohol. It should be kept in well-stoppered bottles.

Zinc acetate is practically a duplicate of the sulphate; but its use has been rather restricted by custom to local application for the purposes of the metallic astringents. Solutions may be employed of the same strength as of the sulphate.

Zinc Valerianate ($Zn[C_5H_9O_2]_2$, H_2O).—The salt is official in the United States Pharmacopœia as *Zinci Valerianas*, Zinc Valerianate. It is in soft, white, pearly scales, permanent in the air. It has a faint odor of valerianic acid, and a taste at first sweet, then styptic and metallic. It dissolves in about 100 parts of cold water and in 40 parts of cold alcohol. Boiling in either solvent determines loss of acid and the formation of a basic salt, with resulting turbidity of the solution. The salt should be kept in small, well-stoppered bottles. From its comparative insolubility, zinc valerianate is locally less active in every way than the salts typified by the chloride and sulphate. Its place in medicine rests upon the idea of combining in one drug the antispasmodic virtues of zinc and valerian; but since the effects of zinc are feeble at best, and valerianic acid is probably not the active principle of valerian root, there is little ground on which to rest a valid claim for the salt's efficacy. This valerianate also has the positive disadvantages of disagreeable smell and taste, and costliness. The salt has been given in doses of from 0.06 to 0.12 gm. (gr. i.–ij.) several times a day, best in pill.

Zinc Phosphide (Zn_3P_2).—This salt is of value solely as a means of giving phosphorus, and has been described under the title *Phosphorus*.

Zinc Nitrate ($Zn[NO_3]_2$, $6H_2O$).—Zinc nitrate forms by the direct action of nitric acid upon metallic zinc. It occurs in colorless prismatic crystals which are soluble in water and alcohol, and are very deliquescent. The salt is fusible, and has been employed, although it is unofficial, in the form of sticks of the fused substance cast in paper moulds, for application to sores and ulcers. The action is caustic and healing, after the manner of silver nitrate. Sticks of zinc nitrate must be kept dry in well-stoppered bottles, else they will be destroyed by deliquescence of the salt.

Zinc Oleate.—An oleate of zinc is obtainable in the form of a fine, soapy-feeling powder, of a pearl color. This powder proves to be a serviceable bland absorbent and detergent for local dusting upon the skin.

Edward Curtis.

ZINC-HEMOL. See *Hemols.*

ZINC, POISONING BY.—The most important salts of zinc, from a medico-legal point of view, are the sulphate and chloride.

Zinc sulphate, or *white vitriol* ($ZnSO_4,7H_2O$), is a colorless salt, crystallizing in small four-sided prisms, which

slowly effloresce in dry air. It is soluble in about two times its weight of water at the ordinary temperature, and in less than its own weight of boiling water; insoluble in alcohol, ether, and chloroform. Its taste is astringent and metallic; its reaction, acid.

Zinc chloride ($ZnCl_2$), commonly called *butter of zinc*, is a soft, white, very deliquescent, readily fusible solid, freely soluble in water and in alcohol. Its taste, in the solid state or in concentrated solution, is acrid and corrosive; in dilute solution, astringent and metallic. Its reaction is acid. When brought into contact with raw surfaces or mucous membranes it acts as a corrosive. It has considerable antiseptic power also, and, in aqueous solution, is frequently used as an antiseptic, deodorizer, and disinfectant. The liquid known under the name of "Sir William Burnett's disinfecting fluid" is such a solution, containing over two hundred grains of the salt in each fluidounce.

Cases of poisoning by these salts have been of rare occurrence and usually the result of accident. Zinc sulphate resembles magnesic sulphate (Epsom salts) very closely in its appearance, and has frequently been taken by mistake for the latter, while Burnett's fluid, which has been the cause of most of the reported cases of poisoning by zinc chloride, has frequently been mistaken for water or other harmless liquid.

Symptoms.—Zinc sulphate acts as an irritant poison, but only when a large quantity has been taken. The symptoms are almost entirely local. The most prominent are: an astringent and metallic taste, burning pain in the œsophagus, stomach, and bowels, nausea, vomiting, purging, dyspnœa, small and frequent pulse, and cold extremities. The intellect usually remains clear.

The symptoms usually make their appearance almost immediately after swallowing the poison; but, in rare cases, they have been more or less delayed.

Wormley quotes a case in which vomiting was delayed for fifteen minutes, and there was no purging for ten hours. In this case a solution containing 46.5 gm. (℥ iss.) of the salt was swallowed. In a case communicated by Lutier active symptoms appeared first after the lapse of fifteen hours.

The symptoms produced by zinc chloride are similar in character to those just described. This salt has, however, a violent corrosive action, which is wanting in the sulphate. The local symptoms are therefore usually more severe than they are in cases of poisoning by the sulphate, and are more frequently followed by symptoms of profound collapse and death. In non-fatal cases recovery may not be complete until after the lapse of several days, or even weeks.

The investigations of C. Ph. Falck, Blake, Letheby, and Harnack show that the salts of zinc paralyze the striated muscles and cause death by their action on the heart and muscles of respiration, without influencing, to any great extent, the central nervous system. F. A. Falck, who experimented with rabbits, found that the temperature of the body is reduced 7°–13° C. in cases of acute zinc poisoning.

Fatal Quantity; Fatal Period.—The quantity of any of the preparations of zinc required to endanger life is not exactly known. The sulphate is not a powerful irritant. In large doses it acts as a prompt emetic, and is frequently rejected by the stomach without producing any other serious symptoms. Quantities varying from 4.3 to 124 gm. (gr. lxvij. to ℥ iv.) have been taken without fatal result. Death has occurred in five hours (a child), thirteen and a half hours (adult, 5.8 gm.), thirty-six hours (7.6 gm.), three days (adult, quantity unknown), and five days (adult, 15.5 gm.). The chloride is much more dangerous than the sulphate. Most of the reported cases of poisoning by this salt have been caused by Burnett's solution, and the quantity taken has usually been known only approximately. Recovery has followed the administration of quantities of this solution varying from half a wineglassful to three fluidounces, the quantity of salt varying, so far as known, from 0.8 to 26 gm. (gr. xij.–cd.). Six and one-half grams (gr. c.) has caused death. Death usually takes place within twenty-four hours. The shortest fatal periods are two hours (Taylor), four hours (Allanson), seven and a half hours (Cousins), ten hours (Letheby). Occasionally the patient has recovered from the primary effects, only to succumb to the secondary effects after the lapse of several weeks. In such cases death usually results from starvation, following upon stricture of the œsophagus, pylorus, or intestines.

Post-mortem Appearances.—When the sulphate has been taken, the lesions are substantially similar in character to those observed in cases of poisoning by other pure irritants. A slight ulceration, near the pyloric end of the stomach, has been noted in a single case. Rarely, there may be contraction of the stomach or intestines.

The chloride of zinc resembles in its action the mineral acids and caustic alkalies. In cases of poisoning by this salt the mucous membranes of the mouth, throat, œsophagus, stomach, and intestines are usually more or less disorganized. In a few cases, however, there has been an absence of corrosion even in the mouth. Perforation of the stomach, and stricture of the œsophagus, pylorus, and intestines may be met with, especially in cases which are not rapidly fatal. Congestion of the brain and its membranes, and of the lungs and kidneys, are usual sequels of acute poisoning.

Treatment.—Vomiting should be encouraged if necessary. Sodic carbonate precipitates zinc carbonate from solutions of soluble zinc salts and may therefore be employed as a temporary chemical antidote. In other respects treatment must be symptomatic.

Other Compounds of Zinc.—The remaining soluble salts of zinc are substantially duplicates, in their effects, of the sulphate or chloride.

Zinc oxide and *zinc carbonate* are white amorphous solids, insoluble in water, but soluble in dilute acids, the carbonate dissolving with effervescence. Either of these compounds, if taken internally in considerable quantity, may dissolve in the fluids of the stomach and intestines and give rise to acute or subacute poisoning, with the usual symptoms of irritant poisoning.

Chronic zinc poisoning has been ascribed to the long-continued inhalation of the vapors of zinc oxide. This form of poisoning has been observed in workers in zinc, brass, and galvanized iron, and is characterized by headache, chilliness, pains in the extremities, a strong metallic taste, nausea, vomiting, diarrhœa, and colic. It is to be borne in mind in this connection that commercial zinc usually contains lead, and frequently arsenic, and that the above symptoms may be those of poisoning by one or the other of these metals, and not by zinc oxide.

The use of galvanized iron pipes for conveying water, and of galvanized iron utensils for the preparation and storage of food, appears to be attended with some danger. Water that has passed through galvanized iron pipes almost always contains zinc compounds, either in solution or in suspension. There is some difference of opinion as to the effect of such water on health, but it is generally believed that the danger of poisoning from the zinc in solution in the water is very slight. When the water has stood in contact with the pipe for several hours it frequently holds in suspension a considerable quantity of insoluble zinc compounds. It seems probable that the use of such water would be attended with danger. As a precautionary measure, therefore, the water that has stood in contact with a galvanized iron pipe for several hours should be allowed to run to waste, or should be filtered before use.

Certain liquids used in cooking, especially such as contain vegetable acids, may dissolve a sufficient quantity of zinc from galvanized iron utensils to produce symptoms of poisoning. Wormley reports a case of zinc poisoning caused by the use of apple butter prepared with cider which had been concentrated in a galvanized iron pan. The concentrated cider was found to contain 1.14 grains zinc oxide to each fluidounce.

Absorption and Elimination.—When compounds of zinc are taken internally the metal is absorbed, presu-

mably in the form of albuminate, and may be detected, after death, in the blood and in all the tissues of the body. Matzkewitsch administered the acetate of zinc to dogs by subcutaneous injection, and found, as the result of five experiments, that the greater proportion of the zinc thus introduced was localized in the muscles and bones. The skin, brain, liver, heart, lungs, kidneys, bladder, stomach, and intestines contained zinc, but in relatively small quantities. Zinc is eliminated with the urine, bile, and milk (Falck, Harnack). According to Michaelis the metal is first detected in the excretions on the fourth or fifth day after the administration of its compounds. The time required for complete elimination is unknown. According to Popoff it can be detected in the urine for months after removal from its influence.

The study of the localization and elimination of zinc is attended with peculiar difficulties, inasmuch as the human system frequently contains small quantities of the metal even when its compounds have not been purposely administered. Raoult and Breton isolated 7 mgm. of zinc from 700 gm. of human liver in one case; 12 mgm. from 400 gm. of liver in a second case. In four other cases they extracted 10, 30, 34, and 76 mgm., respectively, from 1,000 gm. of liver. Lechartier and Bellamy obtained similar results. In one case 1,780 gm. of liver contained 20 mgm. of zinc oxide. The same authors extracted 30 mgm. of zinc oxide from 913 gm. of muscle from the ox, and 20 mgm. from 1,152 gm. hard-boiled egg. They also detected traces of zinc in corn, maize, barley, and white beans.

The frequent presence of small quantities of zinc in the organs of the body may be explained in some cases by the use of water which has been conveyed through galvanized iron pipes, or by the use of food which has absorbed zinc from galvanized iron utensils; in other cases, by the medicinal administration of preparations of zinc before death, or the introduction of embalming fluids containing salts of zinc, after death.

In consideration of the foregoing facts it is obvious that the detection of zinc in the tissues after death cannot, when unsupported by other evidence, be accepted as proof that death was caused by zinc poisoning.

William B. Hills.

ZINGIBER. See *Ginger*.

ZONIAN SPRINGS.—Kane County, Illinois.

These springs are three or four in number, and are located one mile north of the city of Elgin, in a fine, wooded, rolling country, about 2,000 feet above the sea-level. The atmospheric temperature varies from about 75° to 80° F. during the summer, and from 10° to 60° F. during the winter months. The following analysis of the water was made by J. E. Seibel, analytical chemist, Chicago:

One United States gallon contains (solids): Calcium carbonate, gr. 9.56; iron carbonate, gr. 0.49; magnesium carbonate, gr. 2.49; sodium carbonate, gr. 0.45; sodium sulphate, gr. 1.75; sodium carbonate, gr. 0.70; silica and aluminum, gr. 0.26. Total, 15.69 grains.

It is stated that the water also contains a considerable amount of free carbonic acid. The flow of water amounts to about one barrel per minute from each spring. Kidney, stomach, and liver troubles are said to be benefited by the waters.

James K. Crook.

ZYMASE.—In 1897 E. Buchner demonstrated that the phenomena of alcoholic fermentation can be brought about without the presence of living yeast cells or other organized ferments. By subjecting yeast which has been ground up with sand, kieselguhr, and water to a pressure of four hundred to five hundred atmospheres it is possible to collect a fluid free from protoplasmic particles or living matter in any form. When this juice is brought into contact with strong sugar solutions it provokes a vigorous evolution of carbon dioxide (CO_2), alcohol ($C_2H_5.OH$) being simultaneously formed in the mixture. The reaction proceeds unaltered even in the presence of one-per-cent. sodium arsenite or of chloroform and other substances which readily destroy micro-organisms. The activity of the juice is lost by heating above 40°–50° C. From these facts it follows that the reaction is attributable to an enzyme to which the name *zymase* has been given. Despite the vigorous criticism which the announcement of this discovery speedily provoked, it is now firmly established that ordinary alcoholic fermentation is not a "vital" process of the yeast cell, but is brought about by the intermediation of soluble enzymes. The change which sugars undergo in the presence of yeast has always been pointed out as a typical "fermentation" reaction, in distinction from "zymolytic" (enzymatic) transformations. Accordingly the detection of zymase will emphasize more than ever the wide distribution and significance of enzymes in the life processes; and we may almost confidently expect sooner or later to find a specific enzyme for every vital chemical reaction.

Zymase is already known to occur widely in nature. The observations of Buchner on the yeast have repeatedly been verified; Mazé has isolated zymase from fungi; and Stoklasa and his co-workers have demonstrated its occurrence in many of the higher plants like the sugar beet, as well as in various animal tissues. The importance of this for the carbohydrate metabolism and internal respiration of both animals and plants can as yet scarcely be foretold. It is impossible at the present time, however, to assert that the zymases isolated from the various sources referred to are identical. As far as has been investigated the products of the reaction occur very nearly in the proportions demanded by the equation $C_6H_{12}O_6 = 2C_2H_5.OH, + 2CO_2$, only small quantities of side products being found. It seems likely that one of these, lactic acid, owes its existence to the activity of a specific enzyme.

Zymase may be isolated by the method of Buchner and Albert. The intracellular juices obtained by the method already indicated are treated with alcohol and ether, and the precipitate containing the enzyme is dried at a low temperature. The details of the method as applied to various animal and vegetable tissues must be consulted in the original papers. The glycolytic enzyme in animal tissues like the heart, lungs, etc., may also be demonstrated by immersing the sterile tissue in a sterile sugar solution in an atmosphere of hydrogen. The evolution of CO_2 and the formation of alcohol are then readily demonstrated. Experiments of this sort serve to awaken interest in the possible formation of alcohol in the intermediary metabolism of animals.

Although dried preparations of zymase retain their glycolytic properties for a long time, solutions of yeast zymase soon lose their power if a proteolytic enzyme (like yeast endotrypsin) is simultaneously present. Compared with equivalent portions of yeast, the cellular juices containing zymase are less efficient as fermentative agents. This is doubtless attributable to the constantly renewed production of enzyme in the case of the living cells. Zymase may readily be demonstrated in carefully dried yeast in which all the cells are dead. A method for making a permanent sterile preparation of this sort by the use of acetone (Aceton-Dauerhefe) has been devised by Albert.

Lafayette B. Mendel.

LITERATURE.

A review of the literature on the zymase of yeast will be found in Die Zymasegärung, von Ed. und Hans Buchner und Martin Hahn, München, 1903. Further:

E. Buchner: Berichte der Deutschen chemischen Gesellschaft, 1897, xxx. (Discovery of zymase.)

Mazé: Comptes rendus, cxxxv. (Zymase in fungi.)

Stoklasa, Jelinek, and Vitek: Hofmeister's Beiträge zur chemischen Physiologie, 1903, iii., 460. (Zymase in plants.)

Stoklasa and Cerny: Centralblatt für Physiologie, 1903, xvi., 652. (Zymase in animal tissues.)

Stoklasa, Jelinek, and Cerny: *Ibid.*, 712. (Lactic-acid-forming enzyme.)

R. O. Herzog: Zeitschrift für physiologische Chemie, 1903, xxxvii., 381. *Ibid.*

ZYMOGENS.—This generic name has been applied to the precursory stage in which the enzymes are present in the cells of secretory glands. In this condition, there is no activity, but in the process of secretion, or in some in-

stances after the secretion is thrown out upon the mucous surface and has come in contact with activating substances present in other secretions with which it is mixed, the zymogen undergoes a chemical change, the nature of which is unknown, by which the active ferment is formed. Such a conversion into active ferment can also be produced artificially in many instances by treating the fresh gland with very dilute acetic acid, or it occurs spontaneously on allowing the gland to remain for some hours after removal from the body, especially if it be kept during this interval at body temperature.

The presence of zymogens has been known now for many years, and recently great advance has been made in our knowledge of the conditions under which they are set free (see for example, enterokinase, in the article on *Pancreas, Physiology of*).

For further information on zymogens, see the article on *Enzymes.* *Benjamin Moore.*

ZYMOLYSIS.—This is a general term used to designate the changes produced by enzymes. See articles on *Digestion,* on *Enzymes,* and on *Pancreas.* *B. M.*

APPENDIX.

ALASKA.—This vast northwestern possession of the United States, extending over 16 degrees of latitude and 35 degrees of longitude, and embracing 590,884 square miles of territory, equal to nearly one-sixth of the area of the United States, exhibits a variety of climatic conditions and contrasts dependent not only upon latitude, but upon the topography of the country and the influence of the surrounding waters and currents. Two great climatic divisions can be made: southern or temperate Alaska, which can be subdivided into the Sitka, Kadiak, and Aleutian divisions, and northern Alaska or the Yukon district, embracing the vast region to the north and west of the Alaskan Mountains.

The climate of temperate Alaska is characterized by two striking peculiarities: comparative warmth and great moisture, caused by the Kuro Siwo, the "Gulf Stream" of the Pacific. This current crosses the Pacific in about latitude 45° N., and impinges on the coast of British Columbia where it divides, one portion turning northward and westward and the other southward. As a result of this condition, the temperature is greatly modified from what the latitude alone would lead one to expect, exactly as the climate of Great Britain, for example, is modified by the gulf stream. The isotherm of 40° mean annual temperature, that of the lower St. Lawrence valley, is the mean annual isotherm of the Southern Alaskan coast region. Sitka, with a latitude of 57.03°, which is the same as the latitude of Labrador on the Atlantic coast, has a mean annual temperature of 43.9° F., which is only 2.6° lower than that of Portland, Me., and a mean winter temperature of 32.5°, which is 6.9° higher than that of Portland, and only a little less than that of Washington, D. C. The extreme range of temperature is from a point a trifle below zero to 90° above. Similarly, Juneau, in the Sitka district, northeast from Sitka, has a mean annual temperature of 40.9° F. The annexed chart of the maximum, minimum, and mean temperatures of Juneau and Sitka for the year indicate still further the moderate temperature of the region.

The second peculiarity of temperate Alaska is moisture in the form of rain or fog, and in the Sitka division, which extends from Dixon Entrance to William's Sound, the yearly rainfall is from eighty to one hundred and three inches, and there are on an average but sixty-six clear days in the year. "When the sun shines, the atmosphere is remarkably clear, the scenic effects are magnificent, all nature seems to be in holiday attire. But the scene may change very quickly; the sky becomes overcast; the winds increase in force; rain begins to fall; the evergreens sigh ominously, and utter desolation and loneliness prevail." [United States Department of Agriculture, Weather Bureau.] The Sitka district is very mountainous, and the coast bold and steep with few beaches. The mountain sides are densely wooded, and the snow line begins at an elevation of from three thousand to five thousand feet. The prevailing winds being westerly and off the ocean, bring the moisture to the snowy mountains, which condense it. Hence it is the combination of the mountains, the prevailing moist winds from the sea, and the warm Japan current, which results in this enormous rainfall, nowhere else equalled in the United States, the annual rainfall at Sitka being more than double that on the Atlantic coast. At Sitka the rainfall for the three winter months is about thirty inches, and for the three summer months sixteen inches.

The Sitka region is the scenic portion of Alaska, visited by tourists, and here are found immense glaciers descending into the ocean.

The country is heavily wooded with spruce, hemlock, and cedar, and the vegetation is dense. On account of the sparse sunshine agriculture is difficult, but many garden vegetables are successfully grown.

In the Kadiak district, which comprises Cook's Inlet, the peninsula of Alaska, and the Kadiak Islands, the climate is similar to that of the Sitka region, but there is more sunshine and less rain, and the seasonal extremes of temperature are greater. At Kadiak the annual mean temperature is 40.6° F., and the number of days of rain or snow for ten months of the year 1899 was 133, and the number of cloudy days 124, making 257 cloudy and rainy days out of 304. The monthly mean temperature at Kadiak for eight years is as follows:

KADIAK LAT. 57° 48'; LONG. 152 19'. MONTHLY MEAN TEMPERATURE (DEGREES FAHRENHEIT) FOR EIGHT YEARS.

January	30.0	August	55.2
February	28.2	September	50.0
March	32.6	October	42.3
April	36.3	November	34.7
May	43.2	December	30.5
June	49.5	Year	40.6
July	54.7		

In the Aleutian district, comprising the range of Aleutian Islands, the range of temperature is much the same, as the following chart of Unalaska indicates:

UNALASKA LAT. 53° 54'; LONG. 166° 24'. MONTHLY MEAN TEMPERATURE (DEGREES FAHRENHEIT) FOR SIX YEARS.

January	30.0	August	51.9
February	31.9	September	45.5
March	30.4	October	37.6
April	35.6	November	33.6
May	40.9	December	30.1
June	46.3	Year	38.7
July	50.6		

AVERAGE MONTHLY MAXIMUM, MINIMUM, AND MEAN TEMPERATURES (DEGREES FAHRENHEIT) OF JUNEAU AND SITKA FOR THE FOUR YEARS 1899-1902 INCLUSIVE.

	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.
Juneau												
Mean maximum	41.7°	43.0°	50.7°	57.2°	66.2°	73.2°	78.5°	67.7°	63.7°	58.7°	49.6°	47.6°
Mean minimum	9.5	12.0	6.0	29.5	33.2	39.2	44.0	41.7	35.7	27.0	19.3	11.0
Daily mean	29.7	29.1	32.8	40.6	46.6	56.6	57.5	54.2	49.8	43.0	35.9	32.6
Sitka—												
Mean maximum	51.0	47.3	53.6	58.0	64.7	67.7	78.5	65.2	65.0	60.0	54.0	49.7
Mean minimum	23.3	16.3	7.6	28.3	31.2	34.7	40.0	39.7	37.7	30.5	25.3	21.3
Daily mean	35.7	34.3	35.8	42.0	44.6	50.6	55.5	54.4	50.9	45.2	38.0	34.3

According to Harriman (Alaskan expedition), there were at Unalaska only 8 days in the year, during several years' record, which were entirely clear, the remaining 312 being cloudy and 271 of these were rainy or snowy.

The Yukon district, or Northern Alaska, comprises that vast region of the Yukon Valley which extends from the Alaskan Mountains to the Arctic Ocean on the north and Behring Sea and Strait in the west.

In the interior of this region the climate becomes colder and drier—extremely rigorous during the long winter and relatively hot in the short summer. As one continues north arctic conditions of climate begin. On the Behring Sea coast, north of the Aleutians Islands, the winter climate is much more severe than that of temperate Alaska on the Pacific coast, but in summer the difference is less marked. At St. Michaels, on the south side of Norton Sound, the mean summer temperature is 50° F., which is but 4° below that of Sitka; and at Point Barrow, on the Arctic Ocean, the most northerly point in the United States, the mean summer temperature is 36.8° F. Furthermore, the winter on the Behring Sea coast about the mouth of the Yukon River and the Seaward Peninsula is somewhat less protracted and severe than in the interior, although it is still long, and from October to May the temperature rarely rises above the freezing point.

Extreme cold, however, as one knows from the experience of Arctic explorers, is not detrimental to health, and at Nome, the most populous mining town in Alaska, the winter is said to be the most agreeable season of the year, in spite of the fact that in midwinter there are but few hours of daylight, the shortest days giving but about three and a half hours of dusky light. "With hands and feet warmly protected, and winter underwear and windproof outer clothes *and exercise*, one can comfortably weather a degree of cold which, in lower latitudes, would immediately transform him to an icicle. This is due to the dryness of the cold." ("The Land of Nome," by Laurie McKee, New York, 1902.)

The following table, compiled from observations of the United States Weather Bureau, gives the annual and monthly mean temperatures and the extremes for St. Michaels, which is on the southern side of Norton Sound; it also may be utilized for ascertaining approximately the yearly temperature of Cape Nome, which is one hundred and fifty miles distant on the northern shore of Norton Sound, at its junction with Behring Sea. In the same table will be found a statement of the mean number of rainy and snowy days. As will be seen, the rainfall is very light, and is about fourteen inches annually, a striking contrast to that of Southern Alaska.

St. Michaels.

	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Year.
Mean maximum (degs. Fahr.)	33.5°	38.0°	32.0°	40.5°	48.5°	62.5°	77.0°	65.0°	56.0°	47.5°	37.0°	34.0°	....
Mean minimum	−34.0	−20.0	−17.0	−20.5	−7.0	27.0	40.0	37.0	25.0	6.5	- 4.0	−24.0	....
Mean monthly	−8.0	−2.3	8.9	19.9	33.1	46.3	53.6	51.9	43.9	30.5	15.6	4.8	26.1°
Extreme maximum	44.0	41.0	43.0	46.0	57.0	75.0	75.0	69.0	69.0	54.0	42.0	45.0	75.0
Extreme minimum	−47.0	−41.0	−39.0	−27.0	−2.0	22.0	33.0	32.0	18.0	3.0	−24.0	−43.0	−47.0
Mean number of rainy and snowy days	7	4	6	8	9	9	12	14	14	11	9	5	108

From observations made on the Yukon, not far from the site of the gold discoveries, by the United States Coast and Geodetic Survey for a series of six months, the following temperatures are noted: From October, 1889, to April, 1890, the mean temperature was as follows: October, 33° (above zero); November, 8° (above zero); December, 11° (below zero); January, 17° (below zero) February, 15° (below zero); March, 6° (above zero); April, 20° (above zero). "The daily mean temperature fell and remained below the freezing point (32° F.) from November 4th, 1889, to April 21st, 1890, thus giving one hundred and sixty-eight days as the length of the closed season. The lowest temperatures registered dur-

Yukon River at International Boundary, Lat. 65°, Long. 141°.

	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Year.
Mean temperature (degs. Fahr.	−17.0°	−10.0°	7.0°	24.0°	45.0°	57.0°	60 0°	52.0°	39.0°	31.0°	3.0°	−16.0°	23.0°
Extreme maximum	25.0	37.0	38.0	56.0	74.0	84.0	87.0	74.0	66.0	52.0	39.0	17.0	87.0
Extreme minimum	60.0	−55-0	−45.0	−26.0	8.0	30.0	35.0	31.0	14.0	4.0	−35.0	−49.0	−60.0

One cannot be sure of reaching Nome by sea much before the middle of June on account of the ice in Behring Sea, or of getting away from there after the latter part of

ing the winter were: 32 below zero in November, 47 below zero in December; 59° below zero in January; 55° below zero in February; 45° below zero in March; 26° below zero in April. "The greatest continued cold occurred in February, 1890, when the daily mean for five consecutive days was 47° below zero. The weather moderated slightly about the 1st of March, but the temperature still remained below the freezing point. Generally cloudy weather prevailed, there being but three consecutive days, in any month, with clear weather, during the whole winter. Snow fell upon one-third of the days in winter, and a less number in the early spring and late fall months. The change of temperature from winter to summer is rapid owing to the great increase in the length of the day." (Bulletin of the United States Weather Bureau, July 29th, 1897.)

Harriman (Alaska expedition) says that the mean temperature of the warmest month on the Yukon, in latitude 64° 41′, was 4° higher than at Sitka over five hundred miles farther south; but while at Sitka the extreme range of temperature is 90°, it will be seen from the above table that on the Yukon it is 147°.

"With a claim to have seen many distant lands," says Professor Heilprin, "I can truthfully say that never before had it been my fortune to experience such a succession of wonderful summer days as during my stay in the region about Dawson. From August 6th to September 20th, barring three days of partial rain, and perhaps a fourth of cloudiness and mist, the weather was simply perfection—a genial, steady, mild summer, with a temperature rising at its highest to about 80° or 82° F. in the shade."

The average annual rainfall is given as from ten to twenty-five inches, and, according to the authority just quoted, the weather is bright and sunny, and there is practically no fog. "There is more sunshine," says Harriman, "in a month (in the interior) than at Sitka in a year."

Such a climate, although severe, is said to be a healthy and invigorating one to most people, for the cold is uniform and dry, and there is very little wind, a contrast, in this respect, to Nome. In a report by Capt. W. P. Richardson, Eighth Infantry, U. S. A., the fact is stated that when the thermometer rises to zero, as it sometimes does in midwinter, it is too warm for comfortable travel. The best temperature, he states, is from 10° to 25° or 30° below zero. "With this temperature the sleds run easily, dogs work with spirit, and one can exercise with the warm clothing necessary at all times in Alaska without discomfort." The ground is frozen deeply, and in the warmest season only thaws to the depth of a foot or two.

The vegetation in the Klondike region is, comparatively speaking, far more luxuriant than at Nome, where it is of arctic character, chiefly mosses and lichens, and the tundra or thick peat moss, or grass which renders foot travelling wearisome and slow. In the Klondike region the country is well wooded, principally with the spruce, although the aspen, birch, balsam, and poplar are found, and this region of forest extends with breaks several hundred miles northward of Dawson. In the summer the country is green and variegated, with a rich flora. Grass grows abundantly, and all the hardy vegetables are said to grow without trouble. Grain, vegetables, and fruit have been raised in small quantities. The native strawberry is found in many parts of the Yukon valley, and so also are various native berries, especially the blueberry. In the Yukon valley, near Dawson, celery, lettuce, potatoes, turnips, etc., have been successfully grown, as well as oats and wheat, and this in a latitude which runs through Greenland and Iceland! Of course such results would be impossible were it not for the fact that the summer days, though few, are very hot and the sun is almost continually above the horizon.

Fish, furs, and gold are the principal industries of Alaska. The discovery of gold has naturally attracted the most attention, but the fisheries form one of the most important industries, and next in importance to the fur trade is the salmon industry. The population was 63,592 at the census of 1900, of which number over 45,000 were males and about half were whites.

Nome City is the largest town, with a population of over 12,000, and next comes Skagway, with a little over 3,000. Dawson, the principal town of the Klondike region, in Canadian Territory, had in 1899 16,000 inhabitants.

The testimony is somewhat conflicting regarding the mosquitoes, but they are apparently pretty abundant, and at certain times and places constitute a veritable scourge. The gnats are also very annoying.

The accommodations, especially in the mining towns, are naturally not of the best, and are expensive; still, any one possessed of robust health need not be deterred either by the climate or by the poor accommodations from a journey to, or a permanent abode in, Alaska. The steamer accommodations from San Francisco, Seattle, or Vancouver are by some lines quite satisfactory. A summer excursion to the southeastern coast of Alaska—the iceberg region—is a favorite one.

References.—Various government reports from the Interior Department; Department of Commerce and Labor; Department of Agriculture, and the Weather Bureau; yearly reports of the governor of Alaska; Harriman, "Alaska Expedition"; Heilprin's "Alaska and the Klondike"; "The Land of Nome," by Laurie McKee; "The Pacific Coast Pilot," and many other special works.

Edward O. Otis.

ARSENIC, POISONING BY.—It has been estimated that of all the recorded deaths due to poisoning, at least three-fourths have probably been due to arsenic in some form. So powerful a factor has this poison proved in the history of the world's progress, and so instructive are the records, that a glance at the past seems necessary.

The knowledge of the poisonous nature of the compounds of arsenic seems to have first come from out the mysterious East. Long before the dawn of written history the Asiatics, the Egyptians, and doubtless other Eastern peoples, seem to have been well acquainted with the sulphides of arsenic and probably also with the method of preparing the trioxide by roasting arsenical ores. The oldest of the manuscripts and papyri dealing with materia medica, etc., which have come down to us (the famous Leyden collection), include the name "arsenic" in the list of substances with medicinal or poisonous action. We are ignorant, however, of the part this substance played in the world's drama prior to the first century A.D. But about this period the writings of Dioscorides and of Olympiodorus caused the method for the preparation of the oxide to be well known and its poisonous property to be well understood. From this time on, arsenic trioxide, because of its being colorless, odorless, tasteless, and insidious in its action, became a factor in history. Professional poisoners soon appeared on the stage and succeeded in developing poisoning into an art—if this be not a prostitution of this term. The first of these artists in crime seems to have been Locusta. Attached to the court of Agrippina she caused the death of Claudius by means of arsenic; later, as the tool of Nero, she accomplished the death of Britannicus and threw Rome into consternation and terror. Put to death by Galba in 68 A.D., she was succeeded by an adept disciple, Canidia, who administered arsenic to a large number of victims. From this time on, Italy proved a hotbed for schools of crime in which arsenic was always the chief agent. Until the thirteenth and to a certain extent to the fifteenth century, murder by means of arsenical preparations knew no bounds and overflowed all Europe. Standing forth among the many historical lesser criminals, we have Charles the Bad, King of Navarre, whose remarkable letters patent (fourteenth century), giving directions for the poisoning of his brothers and uncles by means of white arsenic to be mixed with food or wine, are still extant; the Pope Alexander VI., murdering out of revenge those of his cardinals who disagreed with him, and the wealthy cardinals, his friends, in order that he might seize their property, meeting death himself through the

mistake of a servant who gave him a bottle of wine containing arsenic intended for Cardinal Corneto. Alexander left two of his five children, Lucretia and Cæsar Borgia, of hideous memory, demons in human form, to distribute arsenic in all directions. About this time arose the famous Council of Ten of Venice, spreading murder abroad largely through the agency of an adept in the use of arsenic, de Ragubo, the Franciscan.

A century later makes us acquainted with the celebrated "Acqua Toffana," which probably consisted of a solution of arsenic trioxide in aqua cymbalaria, to which a small amount of tincture of cantharides was added. The woman Toffana, living in Palermo and Naples, discoverer and dispenser of this liquid, is credited with the death of over five hundred victims, including several crowned heads and two popes. While she practised her nefarious trade for years unsuspected, the Acqua Toffana struck terror throughout all Italy, and even throughout France and Austria. After her detection she fled for safety to a convent, where for twenty years longer her horrible trade flourished in secret. Upon her final detection and execution La Toffana's clients were supplied with the arsenical fluid by Spara, who had obtained the secret of its preparation from Toffana. Spara sold her preparations under a variety of other names, as, for example, "Manna di S. Nicolas di Bari," "Acquetta di Napoli," etc. Since Spara's clients seem to have been mostly of the middle class, records are lacking as to the extent of her criminal practices. Toffana and Spara also prepared and dispensed another poison even more potent, in which arsenic was combined with putrefactive compounds (the arsenical ptomaïns of Selmi). This preparation, sold under the name of "Acquetta di Peruzia," was prepared by sprinkling the viscera of a freshly killed pig with white arsenic, hanging them up and then collecting in a vessel the drippings of the putrefying material.

France now became the theatre of the great arsenical crimes of history through Catherine de Medici, who brought with her to France arch poisoners from her native land. The court of Louis XIV. was fairly smothered in crime. Among the hundreds of petty poisoners two remarkable women, doubtless the greatest criminals France has ever seen, stand head and shoulders above the rest. The first of these, Marguerite d'Aubray, Marquise de Brinvilliers, angelically beautiful, with winning voice and saint-like appearance, yet addicted to unspeakable vices from a child up, had been taught the methods of mixing arsenic with foods and beverages by her paramour Saint Croix. This woman had set her heart upon inheriting the family estate, and to gain her end it became necessary to cause the death of her father, brothers, and sister. In order to accomplish this she obtained entrance to the great hospitals of Paris under the guise of a Sister of Mercy. Here as a nurse she administered arsenic with food and medicine, noted the effects, going each day to the internes to learn the progress of the disease. Finding that her practices were unsuspected and undetected, she carried her experiments still further by giving arsenic in food to the poor who called at her door, dosing her servants and visiting the hospitals to which they were taken in order to learn the effect. Having at last satisfied herself that she knew the dose and the rate at which the poison should be administered, she proceeded with the execution of her long-planned crime. During a period of over eight months she administered arsenic to her father, thirty times by her own hands and a number of times by a servant. At the end of this period the murder was accomplished by giving a double dose. In a like manner she disposed of two brothers and attempted the life of her sister. If her servants displeased her, a little arsenic, carefully dispensed, put them out of her way. It has been impossible to ascertain the number of her victims, so cunningly did she work. Not only did she use arsenic trioxide alone, but also a carefully compounded mixture of this substance with mercuric chloride. Her crimes being discovered upon the death of Saint Croix, she was tried, found guilty, and executed in July, 1676. Thus it was that the Marquise de Brinvilliers invented the infamous "poudre de succession," which in the hands of the second of the women, La Voisin and her accomplices, literally powdered Paris and part of France with arsenic.

The revolting story of La Voisin is foreign to the topic under discussion. Suffice it to say that the poison she dispensed was generally white arsenic; but what is noteworthy, is that she followed the de Brinvilliers' method, which had been experimentally developed, namely, slow poisoning. Poisoning became such an epidemic in France, following the publicity of these cases, that the notorious special court (La Chambre ardente—Court of Poisoners) was established. This body proceeded so perseveringly, thoroughly, and mercilessly that since 1682 there have been no systematic poisonings by professional poisoners, clubs, or bands. It has been recently stated that in modern times no Locusta, Toffana, nor de Brinvilliers can exist, that the illness of the victims would promptly be diagnosed as arsenical poisoning and the criminal discovered. Unfortunately, this belief is not justified, for there are many cases which demonstrate that slow poisoning by arsenic is not readily diagnosed. Take, for example, the case of the monomaniac Hélène Jegado, who from 1833 to 1852 poisoned some 47 persons, about 30 of whom died, all of arsenic poisoning; or again there is the woman Van der Linden, who in 1887, acting as a nurse and at the same time agent for an accident insurance company, poisoned, or attempted to poison, 102 persons. Twenty-seven died; 47 were made seriously ill. As a nurse she dosed her victims, in whose names she herself had made out policies. In due time she collected from the company the amount of the policy for illness or death. So carefully did she proceed that the illness of her victims was not diagnosed as arsenicism. Again, take the cases of great mass-poisoning by wine containing arsenic at Hyères in 1887, due to the circumstance that a wine merchant, with the intention of plastering his wine, had dropped into the fermentation vat by mistake a quantity of white arsenic. There were over 400 victims and 4 deaths. All sorts of diagnoses were made by the physicians, and it was not until many months afterward that the true cause was discovered. Similar errors were made in 1900–02 in the famous beer poisonings in Great Britain. In this epidemic there were over 4,000 victims and 300 deaths. The first cases of illness were reported in the latter part of April and early in May, but it was not until the following November, seven months later, that the proper diagnosis of arsenical poisoning was surely established, and it was shown that the trouble came from impure sulphuric acid used for the inversion of sugar and starch, which materials under the Gladstone bill could be used for the manufacture of beer.

Within a few months two cases of slow poisoning by arsenic have come to the author's attention, in each of which the attending physician failed properly to diagnose the illness. One of these cases was homicidal.

The lessons to be drawn from the historical cases and others cited above seem quite plain. The physical diagnosis of subacute or chronic arsenical poisoning is often uncommonly difficult.

Most Important Compounds with Reference to Poisonings.—*Arsenic trioxide*, As_2O_3 (synonyms: arsenious acid, arsenious anhydride, white arsenic, arsenic, ratsbane, rough-on-rats, etc.) exists in two allotropic modifications, the amorphous and the crystalline. The crystalline form is of a dead white, opaque, and porcelain-like appearance; the amorphous, on the other hand, is clear, transparent, and glass-like, and for this reason is often termed vitreous, and has a tendency to pass slowly into the crystalline state. Because of this change, commercial samples of lump white arsenic are mixtures of the two modifications. Save in India, where it is sometimes colored yellow with cow's urine, arsenic trioxide occurs in commerce as a heavy white powder, or in the form of opaque white lumps, which when broken show a transparent glassy centre. The solubility of the commercial samples varies within quite wide limits; this is due to the fact that the solubility of the two modifica-

tions of As_2O_3 are different, that of the pure crystalline being about 1 in 350 of water at 15° C., and that of the pure amorphous 1 in 108. Cooled from boiling, 1 part in 45 of the crystalline remains in solution and 1 part in 30 of the amorphous. No two observers agree, however, as to the solubility of As_2O_3.

Arsenites.—All the samples of commercial dry arsenite of sodium and of potassium which have been examined by the author seem to correspond most closely to the formulas $NaAsO_2$ and $KAsO_2$. Their solubility in water is quite variable, but is always much greater than that of the trioxide. The majority of cases of poisoning from alkaline arsenites have been from the medicinal preparations of these salts, such as Fowler's solution, etc. Only a very few of these cases have been criminal.

Arsenates.—These salts correspond to the general formula R_3AsO_4. They are of little toxicological interest save for the fact that arsenic acid has been largely used in certain industries (*e.g.*, manufacture of aniline dyes) as an oxidizing agent, and the products placed on the market in an impure condition contain arsenic in enormous quantities.

Sulphides of Arsenic.—The disulphide, As_2S_2, occurs in nature as realgar, and was known to the ancients under the name sandarac or sandaracque. Realgar, both the mineral and the artificial compound, has been used as a pigment, in pyrotechnics, etc. The trisulphide, As_2S_3, long known as the mineral orpiment or auripigment, has had a variety of commercial uses. It was formerly used in printing, in tanning as a depilatory, in medicine, as a pigment, etc. The pentasulphide, As_2S_5, is of no medicinal importance. All the sulphides met with in commerce are amorphous yellow powders, varying in color from a light lemon yellow to a deep golden or even orange tint. When pure they are insoluble in water, hence their toxicity is very low. Some authorities hold that the pure sulphides are not poisonous. Experimental evidence shows, however, that these compounds are acted upon by the fluids of the body, and that arsenic is resorbed. Doubtless a long sojourn of these sulphides in the alimentary canal would lead to serious results. The commercial sulphides are invariably violent poisons, since they contain arsenic trioxide, sometimes to the extent of as much as thirty per cent. Le Prince and Chabenat report the case of a young girl who used an ointment consisting of 65 parts of butter and 35 parts of orpiment as a dressing for a tumor of the breast. Acute arsenic poisoning resulted, with death on the fifth day after the application of the dressing. As a depilatory, orpiment has been used from earliest times. It was a mixture of orpiment with lime or chalk, which was used by the ancients for the removal of the pubic hairs—a practice said to be still extant, at least in the case of women, in certain Mussulman tribes of the East.

Cases of poisoning from organic compounds of arsenic have not yet been reported, if we except those due to the notorious Acquetta di Peruzia. But considerable experimental work has been done on animals with kacodyl, kacodylic acid, diphenylarsine, monophenylarsine, arsendimethylcyanide, etc.

Coloring matters, pigments, containing arsenic, are responsible for a large percentage of cases of poisoning, both acute and chronic. Scheele's green (synonym· mineral green, Swiss green) is copper arsenite of somewhat variable composition. It is insoluble in water, and corresponds to the formulas $CuHAsO_3$ or $Cu_3(AsO_3)_32H_2O$. This beautiful compound is used as a pigment in painting, printing, etc., and as an insecticide. Paris green (synonyms: Vienna green, mitis green, Schweinfurter green) is a double salt, copper aceto-arsenite, corresponding to the formula $Cu\ (As_2O_4)_3,Cu(C_2H_3O_2)_2$. The commercial product is of variable composition according to the method employed in its manufacture. It is now used in enormous quantities as an insecticide; rarely as a pigment in painting, coloring, etc. Aniline dyes of the rosaniline group, which have been made by the old arsenical process, usually contain arsenic in large amount. The most important of these are the magentas and reds, but the blues, violets, purples, etc., may also be arsenical. In fact, it may be said that there is scarcely a shade which cannot be obtained by blending arsenic-containing dyes. Practically all the manufacturers of aniline dyes have now abandoned the arsenical process, but the author is informed that there is still one firm in New York State that uses arsenic acid in the preparation of fuchsin. Closely related to the aniline dyes are the arsenical lakes, such as Cochineal red, Vienna red, etc. King's yellow consists of impure arsenic trisulphide, hence is essentially orpiment. It often contains eighty to ninety per cent. As_2O_3. Mineral blue, a pigment in which copper arsenite and potassium arsenite enter in about equal parts, contains about thirty-nine per cent. arsenic.

Arsenical insecticides are responsible for a large number of deaths, accidental, suicidal, and criminal. Of these substances the most important is Paris green. Its composition and quality are now controlled by statutory enactment in several States of the Union. When sold as an insecticide the statutes call for a product containing combined arsenic in an amount which shall be not less than fifty per cent. calculated as As_2O_3, not over four per cent. of which shall be soluble in cold water. Most of the cases of poisoning by this material occur in the United States and in Russia. London purple (synonyms: English purple, Paris purple), formerly much used, is obtained by treating a by-product of the aniline dye industry with lime. The arsenic is present both as calcium arsenite and as calcium arsenate, the latter in excess of the former. Calculated as arsenic the average amount present in London purple is about twenty-nine per cent. Arsenoids, substitutes for Paris green, have been placed on the market in recent years. Green arsenoid contains on an average about sixty per cent. As_2O_3, and has been incorrectly called Scheele's green. White arsenoid contains barium arsenite; thirty-three per cent. of the arsenic present is water-soluble. Para green is a mixture of Paris green with about thirty-six per cent. gypsum. Laurel green consists essentially of calcium arsenite (thirteen per cent.), gypsum, calcium carbonate, and magnesum carbonate.

Vermin Killers.—Of the many arsenical poisons on the market for the purpose of destroying rats, mice, etc., only one needs discussion, *i.e.*, rough-on-rats. This preparation has been employed in many crimes in the United States and consists of arsenic trioxide about seventy-two per cent., barium carbonate twenty-six per cent., sand two per cent., with usually a little carbon to color it. In case of a question of poisoning by this vermin killer, barium should always be searched for. The author has, however, in his possession a sample of this material purchased some years ago which contains no barium.

Arsenic in Foods, Beverages, etc., occurs (1) as a preservative, (2) in coloring matter added, or (3) as an accidental impurity. In official reports issued by the German Government the claim is made that there are annually exported from the United States to European ports enormous quantities of dried apples which have been treated with weak arsenical solutions to preserve them from decay and from the attacks of insects. Moscow, Russia, suffered severely some years ago from a cholera-like epidemic, the cause of which was eventually traced to sturgeon flesh which had been sprinkled with white arsenic to arrest decomposition. The addition of arsenical colors to foods and beverages has given rise to a large number of cases of arsenical poisoning. Sausage, jellies, preserved fruit, wines, fruit syrups, confectionery, cakes, etc., have all been found to have caused trouble. Usually this has been due to arsenical aniline dyes, but in a few instances Paris green has been present. Accidents arising from the presence of arsenic as an impurity in some product used in the manufacture of the food or beverage are usually confined to beers, ales, or glucose preparations. While we are considering poisonous food materials, the fact must not be overlooked that cattle feeding in the neighborhood of industries throwing out arsenic may become poisoned or else relatively immune from

habitual use, and their flesh when eaten by man may lead to very serious results. The same holds true for milk secreted by an animal which has taken arsenic into its system.

Arsenic in Colored Papers, Inks, Clothing, etc.—Many cases of very serious chronic arsenical poisoning have been traced to these sources. A decade ago the amount of highly arsenical wall papers was appalling, and in spite of the denial of eminent chemists and hygienists, the evidence is such that chronic poisoning from arsenical wall papers must be accepted as an established fact, providing that the room so papered is small, damp, and ill ventilated, and the alleged victim spends much time in the room. Contrary to popular opinion, green-tinted papers are rarely arsenical; those which have caused trouble in the United States have almost invariably been tinted in shades of red. In an investigation conducted by the author some years ago upon an undoubted case of arsenicism from wall paper, it was found that over ninety per cent. of the red and maroon papers obtainable of the same date of manufacture as that on the walls of the room were highly arsenical. Many samples of wall papers manufactured within the last six years have since been examined, but none of these modern papers have thus far been found which contain more than mere traces of arsenic. In all probability the cause of arsenicism from wall papers is largely due to the formation, by moulds and bacteria, of arsine and of a volatile organic arsenic compound. This peculiar action is so well marked in the case of Penicillium brevicaude that advantage is taken of the fact for the purpose of testing for the presence of arsenic. Mucor mucedo, Aspergillus glaucus, Aspergillus virescens also possess this same property, but to a less degree. Colored papers other than wall papers have also given rise to poisoning: as, for example, the chewing of such papers by children, the moistening with the tongue of many colored gummed labels. In 1889 several cashiers in German banks were poisoned through handling with moistened fingers large numbers of Swiss banknotes printed with arsenical ink. Several cases are on record of poisoning from using copying inks, typewriter ribbons and indelible pencils made with arsenical aniline dyes. Graffsky has described several very serious cases of chronic poisoning from handling colored chalk in one of the schools of Germany. A violet-colored crayon was found to contain over seven per cent. arsenic. Clothing dyed with impure aniline colors has been the cause of many a sad case of illness. These cases have usually been caused by such wearing apparel as comes in direct contact with the skin, such as stockings, trousers, waists, etc. In Germany copper arsenite has been used for coloring tarlatan and several cases of serious poisoning have resulted therefrom. Two of the most striking cases of arsenical paralysis with which we are acquainted were due to green tarlatan ball gowns. Zinreck states that he found in twenty yards of this material used for a ball gown 300 gm. of Paris green.

Medicinal preparations have given rise to poisoning, either from overdosage or because of the presence of arsenic as an impurity in the substance administered, as, for example, in bismuth subnitrate and other bismuth preparations, sodium phosphate, glycerin, chloroform, phosphoric acid, sulphuric acid, etc. For the composition and dosage of arsenical medicines, see *Arsenic*, Vol. I., of REFERENCE HANDBOOK.

Industrial poisoning by arsenic is by no means rare, for in a large number of industries the workmen are exposed to compounds of this element in one form or another. In the following table will be found a list of trades or articles manufactured which are credited with cases of arsenicism, and a brief statement of the cause of the illness.

Name of Industry or Article Manufactured.	Causes of Poisoning.
Paints in which the basis is orpiment, copper arsenites, mineral blue, etc.	Arsine, arsenical dust.
White enamel glass, stained glass and certain other glasses.	Arsine, arsenical dust.
Copper, cobalt, nickel, zinc, tin.	Arsenic dust in air from roasting arsenical ores.
Copper refined in the wet way	Arsine.
Hydrogen for balloons, limelights, when made from iron or zinc and an acid.	Arsine.
Phosphoric acid.	Arsenic trioxide.
Sulphur and allied industries.	Arsenical dust, arsine.
Arsenic and arsenical preparations.	Arsenical dust in mines, charging and emptying retorts, handling products.
Galvanized iron, tinned iron.	Arsine.
Zinc chloride.	Arsine.
Copperas (ferrous sulphate).	Arsine.
Aniline dyes by the arsenical method.	Arsenic acid, arsenous acid in dust, in air or on hands.
Artificial flowers, leaves, etc.	Arsenical pigments or dyes by contact, or in dust in air.
Stuffed animals, birds, preparation of natural history specimens.	Arsenic trioxide, arsenical soap and fluids absorbed by hands or in dust.
Bird shot (arsenic used to harden the lead).	Arsenical dust.
Aniline from nitrobenzene.	Arsine.
Indigo blue.	Arsine.
Embalming fluids.	Arsenic trioxide, arsenites of sodium, potassium calcium.
Preservation of wood.	Arsenical dust.
Wall papers, colored papers.	Arsenical dyes and pigments in dust or by handling.

Channels of Introduction.—Accidental poisonings are the result of swallowing the poisonous material, breathing arsine or arsenical dust, or occasionally absorption through wounds or through the sound skin. But in criminal cases every conceivable channel has been used, the usual mode of introduction being in food or drink. A number of cases are recorded in which the poison has been administered to the victims by enemas or vaginal douches. The legend that Ladislas, King of Naples, met his death in 1414 by arsenic introduced into the vagina of his mistress by a jealous courtier, and that Calpurneus murdered his wives by digital introduction of arsenic into the vagina are probably not mere myth and fiction, for we find several modern imitators of Calpurneus. In one instance the arsenical material was introduced by placing the poison under the prepuce, and introducing it into the vagina in this manner, so as to avoid all danger of detection. In another instance three wives were successively murdered by placing in the vagina a mixture of flour and arsenic trioxide. Experiments on animals have shown, beyond the possibility of a doubt, that death may result from arsenical poisoning through such an introduction of the poison into the body. A few cases are found in which arsenical vapors have been employed with criminal intent, as for example the vaporization of arsenic trioxide and the roasting of arsenical pyrites in a room.

Fatal Dose.—Brouardel's investigations have shown that the toxicity of arsenic varies according to: (1) The method of administration; (2) the kind and age of animal; (3) the nature of the food material present in the alimentary canal. Owing to the fact that some persons have, to a certain degree, a natural or acquired resistance to arsenic it is difficult arbitrarily to set any definite figure as representing a fatal dose. Moreover, when the stomach contains a large amount of fatty material a huge dose can apparently be ingested without fatal results. It is to be said in this connection that a very large dose is seldom as dangerous as one consisting of close to what may be said to be the normal fatal dose, for the reason that vomiting is apt to be immediate and the poison is removed at once without having undergone resorption. For As_2O_3 the toxic dose for man can be set as lying between 5 mgm. and 50 mgm. (0.07–0.77 grain), and the fatal dose 100–300 mgm. (1.54–4.63 grains). For Paris green the doses are probably somewhat higher than twice these quantities. The above figures refer to per-os administration. When the poison comes in direct contact with the blood, as for example through wounds, the abraded skin, or the direct introduction into the body by some sharp instrument, it is about ten times as active. Rouyer has attempted to calculate the toxic and fatal doses on the basis of the amount of poison resorbed rather

than the total amount taken. According to his experiments and calculations 0.6 mgm. As_2O_3 resorbed per kilogram body weight will give rise to serious symptoms; 2.5 mgm. per kilogram may cause death in twenty-four to twenty-five hours, while 3 mgm. per kilogram will always cause death in about eight hours. It would seem that Rouyer's figures are probably too high, for they would require the resorption of about 200 mgm. to cause the death of a man of average weight. The actual dose to be ingested would therefore be considerably higher.

In the case of animals we find great variation in the intensity of the action of arsenical compounds, not only with respect to species, but also in different individuals of the same species. Von Gohier has seen a horse remain to all appearances in good health after a dose of 30 gm. of arsenic trioxide, while on the other hand 3 gm. has caused death. Not only do we have this variability of action on different individuals, but veterinarians are fairly well agreed that, particularly in the case of cattle and sheep, an animal may at one time stand a dose as high as 20–30 gm., while the same identical animal will suffer severe illness from 5 gm. at another time. The following table, while necessarily more or less arbitrary, can be taken as probably as nearly in accord with experimental data as is possible with our present knowledge.

	Fatal Dose.	
	When taken internally.	When by wounds.
Horned cattle	10.0 to 30.0 gm.	2.0 gm.
Horses	10.0 to 25.0 gm.	2.0 gm.
Sheep, goats	5.0 to 15.0 gm.	.2 gm.
Swine	.5 to 1.0 gm.	.2 gm.
Dogs	.1 to .2 gm.	.02 gm.
Fowl	.1 to .15 gm.	.01 gm.
Pigeons	.05 to .1 gm.	.005 gm.

It will be seen from the above that sheep and goats are, per kilogram weight, remarkably resistant. A similar resistance is frequently met with in certain dogs.

Habitual Use, Tolerance, Arsenicophagia.—Aside from certain species of fungi and bacteria, arsenical compounds are toxic to all other forms of life. But by repeated small doses a certain immunity is at last acquired, after which enormous doses can be swallowed with impunity. This fact was known in most ancient times, for we are told that Mithridates (first century B.C.), who was well versed in the poison lore of his time, acquired immunity in this manner to protect himself against poisoners. By far the most striking cases of acquired tolerance are to be found among the mountaineers of Tyrol, Styria, Carinthia, the Punjab, and in some parts of the mountain ranges of South America. These mountaineers start taking arsenic, in the form of orpiment or the trioxide, from their youth; the men believing that it enables them to endure greater fatigue, wards off the mountain sickness and makes breathing easier; the women in order to improve their complexion, to acquire shining eyes, a rosy tint, and a well-rounded form. These arsenicophages seem to enjoy perfect health and reach an advanced old age. They exist, however, in a pseudo-normal state, for the suppression of the daily dose of arsenic leads to serious illness. The majority never reach a very high daily consumption of the drug, but instances are not lacking in which the amount taken daily reaches 300–400 mgm. We also have proof positive that certain individuals have taken this same amount at a single dose without suffering any inconvenience thereby. This tolerance and habit seem in many cases to be hereditary. A somewhat similar resistance is met with in patients who have been subjected to arsenical treatment with increasing dosage. After a time considerably over the maximum dose is tolerated. In Europe and in America certain waters are found containing arsenic. These waters have been long used by the inhabitants of the district, but no evil effects have been reported.

The administration of arsenic to horses by grooms in increasing doses has been practised for many years, especially in England, the object being to improve the animal's coat, aid the assimilation of food, and to give them a plump, well-rounded appearance. The arsenic is either mixed with the food or is tied in a tiny piece of cloth and attached to the bit. This latter procedure results in the production of a slight salivation and the appearance of white foam about the mouth, the animal holding its head erect and champing at the bit, conditions which are supposed to indicate a spirited animal. Horses subjected for any length of time to this treatment require a continuance of the daily dose, without which they rapidly lose flesh and condition.

There is as yet no satisfactory explanation for the acquired tolerance of arsenic. The theory that there is an abnormal rate of elimination by the kidneys is not well established, and is insufficient to account for all the facts.

Symptoms. Action.—With the possible exception of the gaseous compounds all other arsenical substances may be said to have a like action on man. No matter, therefore, in what form arsenic is administered the symptoms observed will not differ to any appreciable extent. These symptoms can be grouped under four different heads. Those typical: (1) Of a mineral acid—acidismus. (2) Of a mineral salt—metal toxicosis. (3) Of action on the nervous system: (*a*) splanchnic paralysis, resulting in hyperæmia of all abdominal organs; (*b*) neuritis. (3) Of inflammation of the intestinal tract and of fatty degeneration, especially of the heart. The result of the ingestion of the poison may lead to either acute or chronic poisoning. In acute poisoning it is possible to distinguish three forms: A gastro-enteric or ordinary form, paralysis arsenicalis, and asphyxia arsenicalis.

Acute Poisoning.—Ordinary Form. Soon after swallowing the poison the victim complains of a disagreeable metallic taste in the mouth, of an annoying burning, itching, or tickling dryness of the throat, there being usually frequent spitting and more or less salivation. This is generally, but not always, followed by pain in the upper part of the alimentary canal which gradually passes downward, increasing in severity. In most cases in from one to two hours, rarely later, after swallowing the poison, nausea, vomiting, and purging set in. In the event of Paris green being taken, vomiting sets in at an earlier stage than is the case with other arsenical compounds. The vomited matter may be streaked with blood, or green if copper compounds are present. In a short time the stools which were at first colored with bile, become frequent and rice-water-like. Usually there is tenesmus. The patient finds more or less difficulty in swallowing, suffers from dizziness, headache, pains in the limbs, a burning unquenchable thirst, and often a distressing hiccough. The abdomen is distended and is painful on pressure, the secretion of urine is diminished, and there may even be anuria. The patient's voice becomes hoarse, features pale and haggard, eyes sunken, skin cold and dry. The pulse becomes slow and weak; respiration difficult and oppressed, and death usually takes place in fifteen to twenty-four hours, but often on the second day. The patient is ordinarily conscious to the last, but there may be coma, paralysis, or convulsions. If death does not occur before the second or third day, there is usually an apparent general improvement, save for the persistence of the dryness of the mouth and severe thirst. The temperature remains about normal or very little above. There is apt to be extensive erythema or an erysipelas or œdematic swelling which is most marked on the face and genitals, but there are patches more or less scattered over the body. There may be falling out of the hair. Blebs or pustules may appear on various parts of the body, or there may be circumscribed efflorescences. In many instances recovery is difficult and very protracted. Arsenical applications to the sensitive skin ordinarily give rise to severe dermatoses; as, for example, arsenical eczema of the legs and thighs from contact with trousers or stockings colored with arsenical aniline dyes. There may even be gangrene.

Arsenical paralysis is seen in both acute and chronic

poisoning, but an extensive paralysis is rare. Seisser in the famous Würtemberg mass poisoning observed only 1 case in 373. Alexander has collected the records of 55 cases of arsenical paralysis, of these 17 resulted from chronic arsenicism, while 38 were acute. In the great mass-poisoning in Great Britain in 1900, a very large proportion seem to have been troubled with paralytic symptoms. When arsenical paralysis results from acute poisoning it does not usually appear prior to the fourth day, or even the end of the first week. The normal termination of the seizure is the first half of the second week. The beginning of the trouble is marked by pain and paranæsthesia; soon there is numbness of the hands and feet, extending to the forearm and lower leg; very rarely is the paralysis of greater extent. Pain, which is seldom absent, may be very severe (anæsthesia dolorosa); it may be either constant or intermittent. The paranæsthesia has been variously designated by patients as a "sleepy," "furry," "itching," or "tingling" sensation. The hands and feet are cold, the tactile sense is disturbed as well as the temperature sense, cold water is mistaken for warm, while hot water is not recognized as such. As a rule loss of motility follows in a few days, but may also occur simultaneously with the paranæsthesia. In the majority of cases the patient cannot walk or stand for weeks, or even months, after the attack, but occasionally the effects soon disappear. The muscles first and chiefly affected are the extensors and abductors of the toes, later those of the fingers, and finally those of the lower and upper limbs. According to the investigations of Imbert-Gonebeyre the paralysis may be confined to the knees and elbows. Following the paralysis there is increasing muscular atrophy, which may reach an extraordinary degree of severity. Von Marik has described a case in which almost all the body muscles were affected.

Paralysis arsenicalis may be confused with tabes, alcohol neuritis, syringomyelitis, etc.

Asphyxia arsenicalis is a term given by several authorities to rare cases of exceptionally acute arsenic poisoning with unusually rapid death. In this form there is extraordinarily severe intestinal catarrh with vomiting, diarrhœa with rice-water stools, tenesmus, tonic convulsions first of the lower limbs, later of the upper limbs, cyanosis and death, with marked paralysis of the muscles of respiration in a few hours. This form of poisoning bears a striking resemblance to cholera asiatica of malignant type.

Chronic poisoning is seen most often in workmen in the metallurgical industries, in dye and paint works, among taxidermists, etc. A detailed list has already been given. Hill has also recorded a very unusual case, the alleged result of burning gas made from coal very high in arsenic.

According to Brouardel and Pouchet, who have made one of the most careful studies of arsenicism, there are four distinct phases in the progress of the disease. These phases correspond quite closely to the grouping given above under acute poisoning, but are more marked. The early stages of the disease can be characterized as protracted gastro-enteric catarrh. There are loss of appetite and vomiting of mucus and bile. Vomiting and pain may, however, be absent. The patient is apt to suffer from headache, faintness, irregularity of the bowels, depression, and loss of sleep. The breath is fetid, and the perspiration exhales an alliaceous odor like that of arsine. There is great emaciation. Fever and œdema may or may not appear. The urine is albuminous, contains hyaline cylinders, and substances reducing Fehling's solution. Sugar is rarely present. The urine contains arsenic, and on standing deposits magnesium-ammonium arsenate. A common accompanying symptom of much diagnostic value is obstinate conjunctivitis, together with redness and burning of the eyelids, and defective tear secretion. The throat and nasal passages are sometimes dry and irritated. The voice is hoarse. There may be slight cough, which, in cases arising from breathing arsenical dust, passes into more or less severe bronchitis. At other times the victims suffer from an influenza-like snuffle and the nasal secretions are flecked with blood. Many cases of arsenicism have been diagnosed as "grippe," "cold in the head," etc. The skin is far more severely affected than in acute poisoning. There is generally urticaria or an erythematous eruption, or desquamation. Sometimes papules or vesicles form on the breast, back, and face, while later pustules may appear in the arm pits, upon the scrotum, or in the vulva. Frequently the face takes on a dusky tint, and there is marked pigmentation of most of the exposed parts and the pressure areas of the body, or this pigmentation is confined to the knees, about the neck, and to the region of the stomach. The victim appears to be dirty. So dirt-like is this pigmentation that patients upon their admission to hospitals have been given several successive baths. The hair first turns gray, then falls. There may be growths on the nails; the latter may even be shed. Hyperkeratosis of the hands and feet of short duration is seen in not a few cases. Following the typical symptoms of cachexia and muscular atrophy there is wasting away of the muscles, especially of the lower limbs, though the arms may also be affected and the hands become claw-like. Icterus is neither constant nor characteristic, yet is frequently observed. It never reaches the intensity met with in poisoning by phosphorus. True paralysis arsenicalis seems to be of less frequence in chronic poisoning than in acute; but if it does appear its effects are of greater duration, lasting even a life-time. There are often hemianæsthesia and hemiplegia. According to the reports of cases of poisoning from arsenical beer, published in the *Lancet* in 1900–02, it would appear that a large percentage of the victims suffered from more or less marked paralysis, as shown by difficulty in walking, numbness, pricking, tickling, etc., of the lower limbs from the knees down, and from the elbows down, often accompanied by exquisite pain.

Mackensie has reported cases marked by paralysis of the vocal cords. Another peculiar form of paralysis has been studied by Charcot and Biett, and has received the designation anaphrodisia arsenicalis, because of the fact that the disease is characterized by a paralysis of the nerves of sexual sensation. Five typical cases are known. The physical diagnosis of chronic arsenical poisoning is very difficult. The most reliable method of reaching a decision consists in testing the urine for arsenic. This chemical diagnosis must never be omitted. The fatal period in chronic poisoning is too variable to permit of any statement.

Poisoning by arsenic may sometimes be confused with poisoning by phosphorus, antimony, ricinus, croton, abrus, robinia, podophyllum, etc.

Elimination of arsenic takes place chiefly by the kidneys; but there is reason to believe that in addition to the urine, the bile, milk, and perspiratory fluid play an important part, and that a certain portion of the poison is still further thrown out through the intestines. Arsenic can be detected in the urine in from two to eight hours after resorption, and is usually completely eliminated from the body, save from the bones, in from eight to twenty days. The normal period of elimination seems to be from twelve to fifteen days. This holds true only for acute poisoning, since in chronic poisoning, followed by recovery, the liver seems to retain arsenic for a long period; just how long is not known, but in animals it has been shown to be beyond forty days after the ingestion of arsenic ceased. Wood asserts that he has found arsenic eliminated eighty to ninety days after ingestion. On the other hand, Kunkle reports a case of poisoning by copper arsenite followed by death in seventeen hours, yet no arsenic could be detected in the liver, the stomach, or the intestines.

Saveri has shown that the arsenic eliminated by the urine is in the arsenous condition. Selmi has gone a step farther and has shown that part at least of the arsenic is eliminated in combination with organic matter as an arsenical organic compound, and that doubtless another portion of the arsenic is eliminated as arsine. The question of the elimination of arsenic through the milk is one

of very great importance. In the light of experimental evidence and of cases collected, it is now possible to assert positively that an infant nursing at the breast may die of arsenical poisoning when its mother is undergoing arsenical treatment, or has swallowed some arsenical compound yet not in sufficient amount to give rise to ill ness of the mother; or, in case of a toxic dose having been ingested, there may be death of the infant before the appearance of symptoms of poisoning in the mother.

For information as to the localization of arsenic and its distribution in the body after death, the reader is referred to Vol. VI., p. 722, of the REFERENCE HANDBOOK.

Post-mortem Appearances.—In acute poisoning the findings are but slightly characteristic. In rare cases negative results will be obtained, but only when death has been unusually rapid, as for example in cases of arsenical asphyxia. No matter through what channel the poison has been introduced, the mucosa of the stomach and intestines will generally be found to be swollen, covered with bloody foam, more or less uniformly red, intensely inflamed, or hemorrhagic. In some cases there is ulceration, even necrosis. A few cases of perforation are known. Corrosion may take place in a few hours (five or six), and after ten hours may be very severe; this may not be confined to the stomach alone, but may be seen in the intestines. The small intestine is commonly more or less filled with colorless, watery, offensive contents, while the large intestine contains fæcal matter colored with bile. The liver, though apparently normal, shows on section marked fatty degeneration. Similar conditions obtain in the kidneys and heart. The blood shows no specially marked change, but its alkalinity is greatly decreased. In all but a few cases there is a remarkable preservation of the body with the internal organs fresh and of almost life-like consistence, or there may be mummification. Either of these conditions existing in an exhumed unembalmed body should lead to a strong presumption of death by arsenic, but the practitioner must never lose sight of the fact that preservation and mummification are far from being constant or peculiar to this poison. In deaths following chronic poisoning the findings are quite uncertain. The most constant are atrophy of the muscles, a dusky skin often marked with blackish patches, alopecia, gastro-adenitis, and hepatic, renal, and cardiac steatosis.

The *mechanism* or action of arsenic compounds can be briefly summed up as follows: (1) Local cauterization; (2) vaso-motor paralysis of splanchnics; (3) degeneration of albumin of the body and disturbance of metabolism; (4) disturbance of activity of the central nervous system and of the skin; (5) paralysis of the heart.

Following the paralysis of the peripheral extremities of the splanchnic nerves there results great hyperæmia of the abdominal organs, giving rise to an appearance of inflammation. This condition extending to the mucosa becomes severe gastro-enteritis, explaining why it is that these lesions are seen, no matter what may have been the mode of entry of the poison. The disturbance of the metabolism leads to fatty degeneration of most of the internal organs, and especially of the glands. When this steatosis affects the walls of the blood-vessels, multiple hemorrhage results. As an immediate consequence of fatty degeneration of the heart muscles the ganglia become affected and cardiac paralysis results. The severe cerebral disturbances sometimes seen can be ascribed in part to the sinking of the blood pressure, and in part to degeneration of the ganglionic cells of the brain.

Normal Arsenic.—The question as to whether arsenic is a normal constituent of the body has been the subject of several investigations within the last few years. The weight of evidence seems to support the theory of Armand Gautier, that arsenic is always to be found in the healthy body at least in the thyroid, where it plays an important part, and in the hair, nails, bones, and mammary glands, and that this normal arsenic is eliminated chiefly by the skin and the milk. Before this theory can be accepted as proved more research is needed.

ANTIDOTES. TREATMENT.—The most effective antidote with which we are now acquainted—freshly precipitated ferric hydrate—was first proposed by Bunsen in 1834. It depends for its efficacy upon the fact that it unites with arsenous acid, arsenites, or arsenates to form insoluble compounds. With arsenous acid or arsenites a basic ferric arsenite results, mixed with a variable proportion of basic ferrous arsenite, while with arsenates a basic ferric arsenate is formed. The ferric hydrate must be freshly prepared, since it soon loses the power to unite to form an insoluble compound. The official method of preparation is as follows: To ammonia water (U. S. P.), 110 c.c., add water 250 c.c.; to solution ferric sulphate (U. S. P.), 100 c.c., add water 1,000 c.c. Pour with constant stirring the solution of ferric sulphate into the ammonia water, pour the mixture on a muslin filter, squeeze, and add to the precipitate sufficient water to make about 250 gm. Of this final preparation administer to an adult two to four tablespoonfuls every ten minutes. The dose for a child is one dessertspoonful every ten minutes. Hydrated magnesium oxide, proposed by Bussy in 1846, is also of much value. Like the iron antidote it must be freshly prepared. One part of freshly burnt magnesium oxide is suspended in twenty parts of water. Of this preparation four to six tablespoonfuls may be administered every fifteen minutes. As in the case of iron, insoluble basic arsenites and arsenates result. In Europe the two above antidotes are combined, as, for example. To Liquor ferri sulph. oxydat. (P. G.) 100 gm., add water, 250 gm. To water, 250 gm., add magnesia usta, 15 gm. Mix the two solutions, shake well, and throw upon muslin.

Both the iron and magnesium compounds must be removed from the stomach as soon as possible, since the insolubilized arsenic may be again resorbed through the solvent action of the fluids of the body. A recommendable procedure is to wash out the stomach with water holding magnesium oxide in suspension; then administer the antidote. After a few minutes induce vomiting, or use the stomach pump. Repeat this process several times. Demulcent drinks should be promptly given to retard resorption—milk, albumen in water, flour and water, etc. Following the antidote, the treatment must be symptomatic. It must never be forgotten that during convalescence the diet must be watched with great care, and only bland articles given.

In the absence of the above-mentioned antidotes, ferric hydrate, prepared in any way, can be given, or the following may be employed with more or less success: saccharate of iron, acetate of iron, citrate of iron, dialyzed iron, powdered or reduced iron, milk of lime, sulphur, sulphide of iron, etc. The administration of alkalies must be carefully avoided.

POISONING BY ARSINE is probably of greater frequency in the industries than is generally believed, though acute poisonings are quite rare. Arsine or arseniureted hydrogen is a heavy colorless gas of peculiar fetid odor. Its specific gravity is about 2.7. It is but slightly soluble in water, and burns with a characteristic bluish-white flame. The pure gas is a frightfully active poison, only a whiff or two causing death. Of some twenty cases of acute poisoning on record, practically all have been the result of chemical laboratory accidents, but subacute and chronic poisonings are frequent in the industries where small amounts of arsine are breathed in the air of ill-ventilated work-rooms. Although the odor of arsine is characteristic and very penetrating, the gas may be present in the air of a room in sufficient amount to lead eventually to poisoning, and still not be detected by the sense of smell, or at least not noticed. Poisoning occurs chiefly in the preparation of hydrogen and the manufacture of balloons or toy balloons; in the coloring or bronzing of brass and other alloys; in the desilvering of lead and subsequent treatment of the silver zinc with acids; in the galvanizing and tinning of sheet iron; in the reduction of nitrobenzene, etc., in the aniline industry; in the manufacture of many salts; in fact, in all industries or operations where hydrogen is given off in reactions between compounds containing arsenic as an impurity. Besides these sources there is the further possibility of

poisoning from wall papers in damp, ill-ventilated rooms through the formation of arsine by fungi and bacteria.

In strictly chronic poisoning the specific action of the poison manifests itself in anæmia or pernicious anæmia.

The effects of arsine on the system appear slowly. The victim shivers, complains of chills, and often of an indescribable feeling of sickness passing into great uneasiness and fear, resulting in exhaustion, weakness, and repeated fainting fits, during which the body is cyanotic, cold, and bathed in cold sweat. There is a blackness before the eyes and the pupils are dilated. There may or may not be nausea and vomiting. The pulse is somewhat accelerated but small and weak. Respiration is dyspnœic. The breath and mouth are fetid. After eight or ten hours, or even much later, the specific effects of the poison manifest themselves; the red blood corpuscles are destroyed and methæmoglobin is formed. All the urine passed is bloody, deep red, dark brown, or even black. There is sometimes anuria. Polycholia sets in and the skin becomes icteric or dark-colored. The stools are not watery as in arsenicism, but are colored dark with bile. The liver and spleen are swollen and painful on pressure. There are severe headache and a fear of death. Death occurs from œdema of the lungs or from paralysis of the heart. If death does not result the period of convalescence is generally very long. Spectroscopic examination of the blood for bands of methæmoglobin is of great value in diagnosis. These characteristic bands will also be noted after death, providing that an examination is promptly made.

The treatment of cases of arsine poisoning is difficult and unsatisfactory. Sodium bicarbonate should be administered to convert the methæmoglobin into alkaline methæmoglobin, which the body can readily change to oxyhæmoglobin. Transfusion of blood may often be imperative. The clogging of the canals of the kidneys has been successfully treated by injection of normal salt solution. The remaining treatment must be symptomatic. In the choice of stimulants to counteract the severe depression of the heart's action it should be remembered that alcohol is barred because of its action on the kidneys.

Clinical Tests.—For the rapid detection of arsenic in the urine, vomited matter, stools, etc., where much organic matter is present, there is nothing superior to the Reinsch method, *i.e.*, acidification with pure HCl and boiling with a tiny strip of pure copper foil or gauze. The stained copper should then be tested by heating in a glass tube in contact with air and the crystalline sublimate of As_2O_3 examined with a hand lens or microscope. For inorganic material the modified Gutzeit test will be found to be rapid and reliable. The gases evolved by the action of sulphuric or hydrochloric acid on zinc in the presence of a solution of the material to be tested are passed through cotton moistened with lead acetate (to hold back any hydrogen sulphide), and are tested either with filter paper moistened with mercuric chloride or with a dry crystal of silver nitrate. In the presence of arsenic the mercuric chloride spot turns brick-red, orange, or brown; the silver nitrate crystal first canary or lemon-yellow, then black. *Emile Monnin Chamot.*

ASIATIC CHOLERA.—(Synonyms: Epidemic cholera, Cholera asphyxia, Algid cholera, Malignant cholera, Cholera spasmodica, Pestilential cholera, Pestilential asphyxia, Oriental cholera, Choleric pestilence, Indian cholera, Ganglionitis peripherica et medullaris, Trisplanchnia, Hyperanthraxis, Morbus oryzeus [because supposed by Tytler to be due to damaged rice], Troussegalant, Cholera gravior, Vishucki or Vishuchiki [by Hindoo physicians], Haouwa [tornado] in Bagdad.) (For a wider discussion of terminology, see Macpherson, "Annals of Cholera," chapter ii., ed. 1884.)

The derivation of the word cholera is usually from χολὴ ῥεῦ (flow of bile), or χολὰς ῥεῦ (intestinal flux), but the correct one is probably that given by Jobard, of Brussels (*Gaz. Méd. de Paris*, 1832, p. 389), who considers the term to be made up from two Hebrew words, choli-ra (or morbus malus).

Asiatic, or epidemic, cholera is an acute infectious disease that is endemic in certain parts of India, and that has during the last century advanced out of that country to other parts of the world, where, in its epidemic form, it has produced great loss of life. It is characterized by its great fatality among the communities to which it may be transported, by the apparent ease with which it has been carried from place to place, and by its invariably following the lines of travel in its march from one place to another. It is distinctly a disease of the gastro-intestinal tract, produced, primarily, by a micro-organism and attended with secondary symptoms, due to the absorption of toxic principles elaborated during the development of this micro-organism.

There is only a difference of degree between cholera, choleraic diarrhœa, and cholerine—the disease is the same in all these forms provided that they are accompanied by the activity of the spirillum of Koch. So far as true cholera and cholera nostras are concerned, there is a very great similarity, or rather there may be, between the clinical symptoms of the two diseases, but the differentiation may be easily made by the isolation of the specific spirillum of the former. The same thing is true in regard to the differentiation of true cholera from an attack of indigestion, which, if severe enough, may take on many of the characteristics of true cholera. Cholera nostras is a seasonal disease and is not transportable, and it has been known for ages. True cholera made its first advance out of India in 1817, and since that time has been seen periodically in Europe. In all cases it has followed the line of travel, and has never been seen to be distributed in any other way. Therefore true cholera never makes its appearance except after other cases have been seen that might excite suspicion, while cholera nostras appears only in hot weather, in sporadic cases, and dies out if the weather becomes cooler.

The period of cyanotic chills, although one of the most striking in both diseases, gives no special indications for differential diagnosis, for the same thing is seen as an accompaniment of many other diseases, as acute catarrhal diarrhœas, acute poisonings, etc. The prodromic period exists in cholera nostras practically always, but not nearly always in true cholera.

The period of reaction is of importance in differential diagnosis. In cholera nostras it is usually benign—if the patient escapes the violence of the first attack, convalescence is as a rule easy and rapid; with true cholera, on the contrary, convalescence is exceedingly dangerous—full of pitfalls, and may terminate fatally at any time.

Mention of the disease is made in Sanscrit and Chinese writings. It is spoken of by Hippocrates (Epidemics), and successively by Aretæus, Celsus, Galen, Caelius Aurelianus, Aëtius, Paulus Æginatus, and Alexander de Tralles. All of these writers, with many others, refer to affections resembling the cholera, but it is not until the seventeenth and eighteenth centuries that we find descriptions of the *epidemic* disease. Genuine epidemics, analogous to cholera, are described by Rivière, who made his observations at Nimes in 1564, and by Zacutus Lusitanus, who saw several in different parts of Europe in 1600. The most remarkable accounts by authors of this epoch are those of Willis ("Opera Gen.," 1680, t. xi., p. 74), describing epidemics in London, in 1670, of what he called "dysenterica aquosa epidemica," of Thomas Sydenham, in 1669-76 ("Oper. Med.," Geneva, 1723, pp. 106 and 184), and of Torti ("Therap. Spec.," liv. iii., cap. ii., and liv. iv., cap. j.). Bontius ("De Medic. Indorum.," Lugd. Batav., 1642, p. 136), Delon ("Voyage aux Indes Orient.," Amsterdam, 1684), and Thevenot ("Voyage aux Indes Orientales," Paris, 1689, tom. iii.) observed and described epidemic cholera in India. In 1761, Donald Monro ("An Account of the Diseases in the British Military Hospital in Germany," London, 1764, p. 97) saw an epidemic of cholera in Westphalia; as did Agton Douglass and Bisset, in 1768, in the north of England and in Scotland. Harlem ("Die Indische Cholera"

1831, t. i, s. 144) quotes many dissertations upon the disease, but it is not until the last century that we have a clear account of the transportation of the disease from place to place. From 1817 it seemed to take on a new power of travelling, and owing to this spread the opportunities for its study have vastly increased. The new methods of intercourse and commerce were probably responsible for the appearance of the disease in Europe—not any new property which it developed.

A study of the history of the epidemics that have occurred outside of India will easily demonstrate the facts in regard to the ways by which the disease is transported from place to place.

History of Epidemics of Cholera and Their Lessons.—The dispute is active as to whether true cholera existed in India before its appearance outside of its limits in 1817, but the probabilities are all in favor of its having done so, epidemics of considerable proportions being reported in the eighteenth century; the especial point that seems to be changed in its nature being that it then seemed to take on the property of migration. Whether this was in reality a new property, or whether, as is much more probable, it was simply brought to the notice of Europeans by their being first attacked by it, is an unsettled question. There is no doubt, however, of the very great influence exerted upon its spread by the great pilgrimages to the various shrines of India; nor is there any doubt that the sole home of true cholera—the one place where it is present all the year in an endemic form—is the delta of the Ganges. There are also certain places in India, Indo-China, China and Japan in which it seems to be present nearly all the time, but it certainly is not endemic in Persia, on the borders of the Caspian Sea, nor in Mecca.

From this one place in which it is endemic, cholera has always been transported to Europe in the steps of the traveller and along the routes of commerce; neither wind, moisture, electricity, nor any of the forces of nature have taken any active part in the actual transportation of the disease, although unfavorable climatic and hygienic conditions, of course, may play a favoring part in the development of the disease, after the arrival of its cause.

Epidemics of Cholera.—Cholera has made five appearances in Europe—in 1830, in 1846, in 1865, in 1884, and in 1892. Each one of these appearances was a great epidemic.

There had been also, in 1823, in Astrachan, a small epidemic of cholera, important because it traced the route that the succeeding invasions would follow. Leaving Persia, where it prevailed in 1822, cholera invaded the southern provinces of Persia, forming the southern shore of the Caspian Sea. After some ravages, it became quiescent during the winter of 1822, to reappear in April, 1823, at Recht. From this city, following the western shore of the Caspian Sea, it crossed the Russian frontier in June, at the little town of Astara. From Astara it reached Lenkoran on the 29th of June. On the 11th of September it was seen at Bakou, and on the 22d at Astrachan, where it soon disappeared.

The First Epidemic.—The epidemic of 1830 had the same origin. Ghilan and Mazanderan, the two Persian provinces before invaded, were attacked in 1829. The disease was quiescent during the winter, but appeared in the spring in Ghilan and in the little port of Enselli, situated several hours' journey from Recht. As in 1822, the cholera followed the western border of the Caspian Sea, and showed itself about the middle of June, 1830, at Salian. Taking here two different directions, on the one side it appeared at Bakou, Kouba, and Derbent, and invaded Astrachan; on the other, following the whole valley of the Koura, it advanced toward Tiflis, passing by Elizabethpol, and spreading throughout the whole of the Caucasus. In this way it reached successively the neighboring regions of Astrachan, and advanced up the Volga. On the 4th of August it was at Saratow, thence extending into Russia, and reached the other European States.

This epidemic, by certain extremely interesting peculiarities, demonstrated from the very first the transportability of cholera.

The Second Epidemic.—In 1846, after having reached Salian by a course identical with the preceding, cholera was seen on November 8th in the city of Chemacka, a short distance from Salian. It was in Bakou and at Derbent in December. Forgotten during the winter, it appeared in April, 1847, in the districts of Derbent and of Kouba, and at Tamir-Khan-Choury. From thence it was transported by sick soldiers to the mineral waters of Kisliar. The disease was disseminated among the Calmucks scattered over the steppes near the Volga.

On July 15th it appeared at Astrachan, and advanced at the same time toward Tiflis. From Tiflis it reached Koutais, and was soon carried to Trebizond.

North of Tiflis, the cholera followed the great military road that crosses the Caucasus at the height of seven thousand feet, and toward the end of July it existed at Stavaropol, on the other slope. (It is to be observed that before reaching Tiflis, the cholera entered Persia by the great routes of travel that pass from Bakou, by Erivan, Natchichievan, Djoufa, Ordoubaz, and on toward Tauris. On the one side it attacked the region of the Black Sea, and invaded all its ports; on the other, it passed through Russia, Germany, France, and Italy.)

A striking thing about these epidemics, aside from the exact places that they attack, is their progress by successive stages—a form of advance that is always the same, and which is a trait common to all the epidemics of cholera that have followed the land route. This second epidemic persisted until 1855.

The Third Epidemic.—The great epidemic of 1865 was the first one appearing by the sea route. It demonstrated that the danger is not localized on the Caspian Sea, but that it is also present on the shore of the Red Sea. Its appearance by this route upset all the doctrines that had been held until that time, and the panic that it produced in Europe resulted in the first conference at Constantinople. It is interesting to follow in some of its phases the course of this epidemic, because its influence has been great. It started from Mecca, having been brought into that city by ships coming from India filled with pilgrims. Toward the end of April it broke out in Mecca and at Medina. The mortality increased very greatly during the three feast days at Arafat. More than thirty thousand of the pilgrims died of cholera, and the progress of the disease showed that *everywhere it accompanied these pilgrims.* Egypt, by reason of its proximity to Mecca, was the first country attacked.

From May 19th to June 10th ten steamers landed from twelve to fifteen thousand pilgrims at Suez. By false declarations from the captains they were passed at Suez, although the *Sydney*, an English steamer, had lost a number of cases during the voyage. The first steamer, landing May 19th at Suez, had thrown its dead into the sea. On the 21st, cases appeared at Suez, and among the number were the captain of the vessel and his wife.

June 2d, the first case appeared at Alexandria, and in two months cholera had four thousand victims in Alexandria, and in Egypt, in less than three months, it produced the death of more than sixty thousand individuals. The foreign population emigrated *en masse*, and carried with them throughout the entire world the germs of the disease. Europeans and Levantines, to the number of from thirty to thirty-five thousand, started for all the ports of the Mediterranean, and cholera developed at Constantinople, at Smyrna, at Beyrout, in Mesopotamia, and at Odessa on the Black Sea, and was carried to New York and Guadaloupe by steamers, *appearing in the port at the same time that the steamer landed its passengers.*

Its importation into New York was as follows: The *Atlanta*, an English ship, left London on October 10th with a cargo of merchandise and forty passengers. The sanitary condition of London was at that time excellent. Reaching Havre on the 11th, where it remained one day only, it embarked five hundred and sixty-four new passengers, mostly Swiss, who had all passed through Paris, where, with certain exceptions, they had remained at

least a short time, and where at the same time cholera was raging with great intensity. Two German families had stayed in Paris at the Hôtel of La Ville de New York, and five days at the hotels of the Weissen Lamm and Hultgarderhof. Some emigrants that had arrived several days before in these last hotels had fallen suddenly ill. The steamer sailed on the 12th, and on the next day there was a death from cholera of a child in the family coming from the Weissen-Lamm Hotel. Five other deaths followed on the 14th, the 16th, the 18th, the 19th, and the 22d, in the family that had stayed at the Hultgarderhof.

On the arrival of the *Atlanta* the surgeon declared 60 cases of cholera, and 15 deaths during the voyage. Two deaths occurred in port, and of the 142 patients sent to the Marine Hospital from November 6th to 19th, 6 died, which makes a total of 23 deaths. The *Atlanta* was immediately isolated in the lower bay, and after ten days of quarantine all the sick were removed, and, thanks to these measures, New York was preserved.

There were also importations in 1866 by the steamers *Virginia* and *England*.

The epidemic of 1865 ceased in 1874, and there was no other case seen in Europe until 1884, although there were interesting manifestations in other countries and on the sea—interesting from the point of view of the transportability of the disease.

The Fourth Epidemic.—The epidemic in Egypt in 1883 was no surprise to those who knew the sanitary condition of the country. Cholera appeared at Damietta toward June 19th or 20th, possibly a little earlier, and its explosion at this time is ascribed, certainly by the French, to the suppression of all sanitary precautions, including quarantine, by authority of the British Government. This epidemic at Damietta increased for about fifteen days, remained stationary for about five or six days, and then diminished just as speedily. It was almost extinct a month after its appearance, having claimed from two thousand to twenty-five hundred victims. The spread of the disease throughout Egypt was manifest and rapid. (An interesting account of how this epidemic reached Damietta is given in Proust's work on the "Defence of Europe against Cholera," Paris, 1892, p. 7.)

Cholera had not yet died out in Egypt, before the news came that it had broken out among the pilgrims to Mecca, and there has been much discussion as to the origin of this epidemic.

In 1884 a number of vessels left the extreme East, and had cases of cholera on board during their voyage; but, by reason of the precautions taken, Egypt and Europe escaped the danger at this time.

The first case of cholera seen at Toulon occurred on June 13th, on the ship *Montebello;* a second case on June 14th; a third on the 18th, on the *Jupiter*, near the *Montebello;* a fourth, also on the 18th, on the *Montebello;* a fifth, June 20th, on the *Alexander*, which was also placed near the *Jupiter* and the *Montebello*. After the 21st the disease spread through different quarters of the city, and it is thus shown that it did not make its appearance at Toulon in the city, but just outside.

Its importation into Marseilles occurred by the appearance of the first case on June 27th, in a young man, who had three days before come from Toulon. The next case, which occurred on June 28th, was that of a man who lived in the same neighborhood; and from this time onward the disease continued to spread.

In Paris there appeared two cases on the 13th or 14th of July, but the epidemic did not really begin until the 4th of November.

In Brittany the first case was not observed until September 20th, at Concarneau. Other ports were successively invaded.

Algeria was attacked in 1884, and there was a slight recurrence in Algeria and in Tunis in 1885.

Cholera was brought to Italy in 1884 by the Italian workmen, who, to the number of more than eight thousand, returned to their country after the extension of the cholera to Toulon and Marseilles. The province of Cuneo, in Piedmont, was the first one attacked, on June 27th, and the disease spread successively to different parts of Italy, to Genoa, Naples, Venice, Sicily, and so on.

It appeared in Spain, in the month of August, in the province of Alicante, and ceased toward the middle of October, reappearing in the middle of February, in the district of Gandia, raging through the month of June to the month of December, 1885, and producing a considerable mortality. It is remarkable that it attacked especially the small towns more than the large cities. The Commune of Aldea de San Miguel, with only five hundred inhabitants, lost more than half of them in thirty-six days.

Cholera also appeared on the Adriatic shores of Croatia, at the end of 1885, and in 1886 on many points of the Austro-Hungarian shore in Istria and in Dalmatia.

The comparison of the mortality in France, Italy, and Spain is interesting. In France and Algeria together there were 13,000 deaths in a population of 39,000,000—1 in 3,000 inhabitants. In Italy there were 35,000 deaths in 26,000,000, that is to say, 1 death in 600 inhabitants. In Spain there were 180,000 deaths, among 17,000,000 inhabitants, that is to say, 1 death in 100 inhabitants. So it appears that Italy was attacked five times more severely by the epidemic than France, and Spain six times more severely than Italy, and thirty to forty times more severely than France.

Much has been said about the immunity of Portugal during the epidemic of 1884 and 1885 in Spain. Many reasons can be brought forward for this, viz., the slight tendency of the Spaniards to take refuge in Portugal, the geographical conditions, and finally, the prophylactic measures taken at the frontier.

In spite of the imperfect quarantine and incoherent measures prescribed by the governments of South America against the vessels coming from Europe, a ship from Genoa, the *Perseo*, carried cholera to Buenos Ayres, and the disease spread into the Argentine Republic, Uruguay, and Chili.

From 1884 to 1886, a period of three years, more than twenty vessels coming from the extreme Orient to Europe, on passing through the Red Sea and the Suez Canal, had, either at the moment of their departure or during the voyage, cases of cholera.

The Cholera of 1889, 1890, 1891, *and* 1892 (*the fifth epidemic*).—In 1890 cholera appeared in Irak-Arabi, in Mesopotamia, in Persia, and in Syria, where it had not been seen for almost twenty years. It had been imported into the region bordering on the Red Sea and into Mecca, where it had not been since 1883, and it was observed in Spain, where it had been extinct since 1885.

In summing up what we know of the origin of cholera in Irak-Arabi and in Mesopotamia in 1889 and 1890, the following must be our conclusions:

It is very difficult to admit that the cholera of Irak-Arabi can be attributed to the revival of the old epidemic of 1871, and if this hypothesis be excluded, we are obliged to accept the idea of importation, and it is only possible to think of one portal of entrance, the Persian Gulf, and one source in India, namely Bombay and its environs.

We know from other sources that during and before the appearance of cholera in Irak-Arabi the mortality of this disease in Bombay and its environs reached the enormous number of more than six hundred deaths a week. The condition of the vessels of the British India Company, that alone regularly frequent the Persian Gulf, bring passengers there, and frequently bring pilgrims from India, has been, to say the least, suspicious. Everything points therefore to the conclusion which bears every appearance of truth that the cholera penetrated into Irak-Arabi through Chat-el-Arab. The importation was performed in this way much more probably than by any other means.

In regard to the epidemic of 1890–91 in Hedjaz, Proust offered to the Committee of Hygiene the following conclusions which were accepted: (1) The cholera of Cameran was imported by an English vessel coming from In-

dia; (2) the cholera of Hedjaz appears to have been brought by the sea route; (3) the pilgrimage to Mecca is a constant menace to the health of Europe; (4) the measures prescribed for the government of the pilgrims to Mecca have not prevented the cholera from developing, and it is therefore necessary to perfect these measures; (5) the prophylactic measures prescribed by the Alexandrian Conference at the time of the return of the pilgrims, have this year prevented the disease from gaining a foothold in Egypt and in Europe. There is reason, therefore, for continuing this conference and for giving it more authority and making it in reality international. There is also reason for increasing the means for isolation and disinfection on the Red Sea.

The epidemic which appeared in Spain in the month of May, 1890, and lasted until the end of November, gave rise to much discussion in regard to its origin, a discussion that reached no final conclusion.

In 1890 cholera also appeared in Japan, beginning in June and lasting throughout the year. Over 46,000 cases were reported. The epidemic of 1892 appeared first in Southern Russia and thence spread to isolated parts in the north of Europe, notably Hamburg, where it continued, with declining severity, into 1893 and 1894.

In September, 1892, 10 cases, with 8 deaths, occurred in New York, being imported from Hamburg, or probably derived from such imported cases, and 73 cases, with 43 deaths, occurred in the harbor, together with 56 suspicious cases of disease thought to be cholera. In 1893, 23 cases, 4 fatal, occurred in the harbor, and one death, verified by bacteriological examination, took place in Jersey City, where there were also 6 deaths following a disease clinically diagnosticated as cholera. Since then no cases have occurred in this country.

In 1895 there were serious epidemics in China and Japan, over 12,000 cases, with over 8,000 deaths, being reported from the latter country.

In 1896 cholera appeared in Russia, Turkey, Egypt, and a few cases in Austria. During the years from 1897 to 1901, inclusive, cholera does not appear to have spread beyond the regions where it is endemic, except a few cases imported from those places.

In 1902 cholera assumed epidemic form in Mecca, Turkey, Russia, Japan, and China. There were also a few cases in Egypt and other southern Mediterranean countries. In the Philippines, between March 20th and the end of October, over 4,200 cases, with more than 3,300 deaths, occurred in Manila, and in the provinces outside of that city over 102,000 cases, with between 66,000 and 67,000 deaths. Since that time, and into 1903, cases of cholera have occurred in these islands. The first case came from Hong-Kong.

Transportability and Means by which the Disease is Transported.—The transportability of the disease is demonstrated by, first, the facts in regard to its propagation after it has been imported; second, by the efficacy of certain measures of prevention; third, by the general march of epidemics of cholera; and fourth, by the development of epidemics in the infected localities.

1. *Propagation.*—Brochard, in "Du Mode de Propagation du Cholera," Paris, 1861, reports a very large number of observations favoring the idea of the transportability of cholera, and the number of instances proving this is so great that they need only to be spoken of to be accepted.

An illustration may be taken from the article by Huette, in the *Arch. Gén. de Méd.*, 5th series, vol. vi., p. 571.

In speaking of cholera in Chatillon, he says that the first case was observed in the Faubourg du Puirault, in a workman, thirty-five years old, who was attacked immediately after his return from Oussoi, where he had gone to take care of his parents who were sick with the disease. His neighbors were very soon attacked, and the epidemic invaded the entire Faubourg du Puirault, where it remained concentrated for some little time. Finally the inhabitants, frightened by the disease, scattered through Chatillon, and the cholera appeared indiscriminately throughout the city. The instance is interesting, because while the inhabitants remained in the Faubourg du Puirault, the disease stayed there; whereas, as soon as they scattered, it spread with them throughout Chatillon.

Another instance, interesting as an example of the transmission of the disease by clothing, is given by the same authority, in speaking of the Commune of Oussoi. Madame Bresson, of the hamlet of Moulineuf, near Oussoi, a precinct free from cholera, received a boarder from Paris, June 27th, who on the next day showed the first symptoms of cholera, and died on July 3d. Some days after, a child of this woman was attacked and died on July 13th. On the same day Madame Bresson herself was taken sick, and died on the 17th, after having been taken care of by two neighbors named Sahan and Moret, who died, one on the 16th and the other on the 24th. The husband of Madame Bresson died on July 26th. Madame Burette, who lived in the extreme end of the hamlet, washed the linen of the two women, Sahan and Moret, and was attacked with cholera. In this way, an epidemic was started that carried off eighteen persons in a very short time. Before the arrival of the person from Paris no case had been observed in this hamlet, that had been spared by the cholera both in 1852 and in 1849. Dr Huette calls attention to the distribution of this hamlet of Moulineuf, which is composed of ten little collections of houses, separated by great distances. No cases of cholera were observed excepting in three of these collections of houses—first, that occupied by the Bresson and Sahan families; second, that occupied by the Moret family; and third, that occupied by the Burette family. The third collection of houses was situated at the extremity of the hamlet. No case of the disease was observed in the other houses, of which the inhabitants had had no connection with these three families.

Proust (*loc. cit.*, p. 165) quotes an occurrence illustrating another series of facts.

In 1854 the French army was collected at Varna, a short distance from the English army. Some detachments remained at Gallipoli, the original place of debarkation. There were, besides, a small Anglo-French force of occupation in the Piræus, and also some detachments at Constantinople. The armies were reinforced practically every day by new arrivals. The sanitary condition was satisfactory in all respects. On July 5th the packet *Alexandre* arrived at Constantinople, having left Marseilles on June 26th with five hundred men of the Fifth Regiment of Light Infantry, coming from Montpellier, and having passed through Avignon, where cholera was raging. It appeared on board, and three men died during the voyage to the Dardanelles. Four cholera patients were landed at the Piræus, where the cholera broke out immediately, and made great ravages. The troops were disembarked at Gallipoli, where two new cases of cholera were immediately sent to the hospital, and the ship, having only a few passengers on board, sailed for Constantinople, where a quarantine was imposed on it. On the other hand, it appeared that previous vessels sailing from Marseilles had already suffered from cholera, and that one of them had landed a patient in the military hospital at Constantinople. On July 15th, after new arrivals of cholera patients, the disease spread at Gallipoli, and there appeared in the military hospital of Constantinople a choleraic focus. Fauvel, struck by the danger, proposed, and had adopted by the Council of Health at Constantinople, a momentary interruption of the communication between Gallipoli and Varna. The measures prescribed were not executed, and in spite of the insistence of Fauvel before the Marshal de Saint Arnaud, many ships sailing from Gallipoli passed the Bosphorus, and went directly to Varna, where free pratique was accorded them. Cholera then broke out in the army among the newly arrived soldiers and in the hospital. On August 5th the epidemic was violent at Varna, especially among the troops sent into the Dobrudscha. The English army was invaded, having the epidemic on board the fleet. In the Crimea, the epidemic,

helped on by the arrival of the fresh troops, continued until 1856.

The importation of cholera into Constantinople in 1865 equally deserves to be spoken of. Constantinople was in an excellent sanitary condition when the frigate *Moukhiri-Sourour* arrived from Alexandria, on June 28th, 1865. She had passed more than five days on the voyage, and therefore, in accordance with the rule that then held, free pratique was granted her, the surgeon having declared that there had been no illness during the voyage; but this declaration was false. The evening of June 28th there were landed from this frigate twelve sick persons, of whom one was attacked with cholera, who died during the night, and eleven were affected with cholerine. It was learned on the next day that during the journey from the Dardanelles to Constantinople two choleraic bodies had been thrown into the sea. On June 30th nine other cases were landed. The ship was sent into quarantine at the mouth of the Black Sea. The patients were transported to the Marine Hospital, near the arsenal, and here one special circumstance should be noted. The road that went from the landing to the hospital being opposite, it was necessary to carry the sick past the barracks occupied by military workmen in the arsenal, and the first indigenous cases of cholera occurred among these workmen, and on board a corvette that was near their barracks. On July 3d one of these military workers was received at the hospital with a choleraic diarrhœa, and on the 5th presented all the symptoms of cholera. That same day a new case was furnished by the workmen, and another on the corvette spoken of above. The barracks were then vacated, and the workmen were placed in tents on the heights of Okmeidan; nevertheless, the disease continued to rage among them, and among the ships collected before the arsenal, and it attacked on the one hand the guard in the interior of this establishment, and on the other the workmen at the Ministry of Marine, situated very near the barracks of the military workmen. On July 8th two cases occurred outside the arsenal, and from July 10th the epidemic commenced to invade the quarter of Kassin-Pacha, near the arsenal, and inhabited by the workmen of whom we have spoken. It then propagated itself throughout the city.

One more instance of the importation of cholera may be given, as illustrating that a single case, carried a great distance by rail, may give rise to an epidemic.

Toward the end of the month of August, in 1865, cholera suddenly broke out at Altenburg, in Saxony, in the centre of Germany. The first case was that of Lady E——, who had left Odessa on August 16th, and had arrived at Altenburg on the 24th, without having stopped on the journey. She travelled with a child of twenty-one months old, who was affected with diarrhœa. She went to her brother's, and sent for a physician to see her child, whose diarrhœa had become very severe. This woman, who was meanwhile well, said that at her departure from Odessa there had not been in that city any disease; but this was an error, for some cases of cholera imported from Constantinople were already in the hospital in the lazaret, and, the day after the departure of this lady, cholera appeared at Odessa. She said also, that having embarked to go up the Danube, everybody appeared to her to be well on board, although the vessel had passed by certain localities where cholera was raging; however that may be, three days after her arrival at Altenburg, on August 27th, and the very same day that the physician had visited her child, this lady fell ill, and the next day the physician recognized all the symptoms of Asiatic cholera. She died on the 29th. On the same day, in the same house, her sister-in-law was attacked, and died on the 30th. The child died on the 31st. From this house the cholera spread into the city and suburbs. The family of a workman, who died on September 13th at Altenburg, carried the disease to Werdeau, and the house occupied by this family was the point of departure of another epidemic that carried off two per cent. of the entire population of the city.

2. *The Transportability of Cholera is Confirmed by the Results of Restrictive Measures.*—We see always that a rigorous sequestration and a rigorous interruption of communication by land or sea, if that be possible, result in preserving certain places or certain countries, and in these facts is a powerful argument against any idea of the transmission of cholera through the air.

In 1867 Messina and the whole of Sicily were entirely free from cholera, and yet vessels coming from infected countries daily passed through the narrow Strait of Messina. And again, during the epidemic of 1856 at Constantinople, the scholars of the Military School, to the number of five hundred, were rigorously sequestrated in the establishment, and escaped the cholera that was raging in the neighborhood; and events that occurred at the lazaret of Fort Genoa, in Algeria, in 1884, demonstrated also the efficacy of isolation in order to prevent the transportation of the disease to the neighboring cities.

3. *Transportability as Shown by the General Progress of Epidemics of Cholera.*—If we look at epidemics as a whole, we see that they always follow the course of human currents of travel. It is in the East, or in the countries bordering upon Europe, that we can best follow the development of this law, because in such places the routes are less frequented, and the demonstration is more striking. In order to pass from Persia into Russia in any way except by the great line of travel passing through Erzeroum, Tauris, and Natchischevan, there are only two ways—that over the Caspian Sea, and the land route that follows the western shore of this sea. Both of these routes pass by Recht, Astara, and Lenkoran, and end both of them at Bakou, and in the same way cholera, in the epidemics of 1823, 1830, and 1846, always and invariably passed through Recht, Astara, Lenkoran, and Bakou. At the latter city the land route splits on the north. It continues to follow the western border of the Caspian Sea, and passes by Derbent, and reaches Astrachan exactly as does the sea route, and we have seen cholera at every one of its appearances, in 1823, 1830, and 1846, travel over this same line, passing by Bakou, Derbent, and Astrachan. In 1823 it stopped at Astrachan, while during 1830 and 1846 Astrachan was only one of the steps of its invading march.

The second line of travel passes over the Caucasus. It leaves Bakou, passes by Tiflis, and follows the Caspian Sea to the Black Sea. The point of departure from the Caspian Sea is Bakou. The point of arrival on the Black Sea is Poti, or Trebizond. The epidemics of 1830 and 1846 divided, following both of the two routes that have been spoken of. One current followed the border of the Caspian Sea, another crossed the Caucasus.

This progress of cholera, always following the same lines, is a striking illustration of the law formulated. It always follows the human currents, in the steps of the traveller. It is imported by man alone, and precisely the same point is shown if we follow the successive steps of the epidemics that have travelled by the sea route.

As an illustration, the epidemic of 1854 in the Crimea was due to vessels coming from Marseilles, and carrying troops from an infected country. Cholera appeared successively at every one of the points where these vessels touched. They landed at Messina, and Sicily was invaded. They touched at the Piræus, and Greece was attacked. They stopped at Gallipoli, and cholera appeared at Gallipoli. Constant communication was being held between Gallipoli and the Dardanelles, Constantinople, and Varna. Cholera developed at all three places. The same was shown in the progress of the epidemic of 1865. It must not be supposed, however, that the assertion is made that cholera took the special direction from east to west; on the contrary, it radiated from India in all directions—north, south, east, and west—according to the ease and number of the means of communication.

4. *Transportability as Indicated by the Evolution of Epidemics in Infected Localities.*—Many examples of this may be quoted, among which are the following:

In Constantinople it is possible to trace out the successive extension of the disease up to the time of its general diffusion. At Constantinople it manifested itself first at

the arsenal, where it had been carried by the sick who were landed from the ship *Mouktare Sourour*. From the arsenal it reached the neighboring quarter of Kassin-Pacha, and then a few cases appeared in different parts of the city, for the most part of persons who had fled from the quarter first attacked. Up to July 16th the total of the deaths from cholera in the entire city, except those at the Marine Hospital, reached one hundred and thirty, when suddenly it was learned that the disease had broken out with violence at Eini-Keni, a village situated on the Bosphorus, twelve or fifteen kilometres from the quarter where the epidemic had begun. It was established that the first case of cholera had appeared on July 11th, in a Turkish café, in a workman coming from Kassin-Pacha; that on the next day many of the individuals who frequented this café fell ill, and two died; that during the following days the disease was propagated in the quarter until the 16th, when, after the occurrence of several deaths among prominent families, a panic seized the whole population of the village, who fled in all directions. Mussulmans, Greeks, Armenians, and Jews fled into other villages and other quarters of the city which were then unaffected, but in which the cholera speedily made its appearance. The Jews in particular, who had been the most seriously attacked, and who carried with them their soiled clothing and their dead, became the special propagating agents of the disease. At Koustoundjouc, at Kas-Keni, and at Balata, the epidemic broke out immediately after the arrival of these fugitives. From this moment dates the generalization of the epidemic. It is not necessary to add other examples. The same thing is shown in the history of every local epidemic that has been intelligently traced.

It has been opposed to this idea of the transportability of cholera that sometimes a restricted intercourse has failed to arrest the progress of the disease; but in all these cases the measures were either tardily employed or applied without scientific rule. Others have spoken of the immunity of countries which had not protected themselves by any sanitary measures. The answer to this is the question, whether cholera, although it is a disease capable of spreading by infection, must, therefore, be possessed of a method of forcing this infection. And, in conclusion, no matter what the differences of opinion are, the law of transportability remains absolutely established by all the facts yet obtained in regard to cholera.

Methods of Transportation of Cholera.—In a consideration of the question of the method of transportation of cholera, we are to look at two principal points, the agent of cholera, that is, the organism of the disease, and second, the medium.

The agent of cholera is unquestionably a bacterium, having India for its origin. It extends itself, and reproduces itself indefinitely, and many media serve as vehicles for its transportation throughout the entire world, but this choleraic agent would be wholly powerless if it did not encounter favorable conditions for its development. The medium, therefore, is indispensable to its power, and this favorable medium is made up of certain telluric conditions, the surroundings, and so on. So far as the methods of transportation of cholera are concerned, therefore, we have to consider more the medium in which it appears than the cause of the disease itself. Fauvel has expressed this truth as follows: "That a fire is not proportionate to the spark which gives it birth, but to the combustibility and mass of the material that it encounters." So, frequently, a few cases, or one only, as at Altenburg, are sufficient to produce the explosion of an epidemic.

The clinical consideration of the means of transportation of cholera is to be made under the following headings:

First, the transportation by men attacked by cholera, and the rôle played by the closets that have received choleraic excreta. A person arriving from an infected place is always necessary for the beginning of an epidemic. In other words, man himself is the most powerful agent for the spread of cholera, the specific microorganism being found, as has been demonstrated by innumerable experiments, in the excreta. Washerwomen have been attacked by the disease after washing linen soiled by evacuations, while others, who had simply touched this linen, also contracted the malady. Budd relates (quoted by Hirsch in *Schmidt's Jahrbücher*, vol. xcii., p. 255) that in 1854 a person affected with cholera arrived in an English factory of six hundred and forty-five workpeople. There followed one hundred and forty-four deaths from cholera in five weeks. The disease developed solely among those who made use of the closets where choleraic dejecta were deposited. Instances of this kind can be multiplied almost indefinitely.

Second, the transportation by means of choleraic diarrhœa. As illustrations of this, innumerable instances might be quoted, especially that mentioned by Budd in the reference given above. A person sick of diarrhœa came into the midst of a perfectly healthy population in a colliery, and died. Diarrhœa became general, and seventeen persons contracted cholera. The case of Dr. Alexander, in the *Gazette Médicale* for 1849, is also an illustration of this point. There was not at Hamel, a village twenty-five kilometres from Amiens, any indication of cholera, when, on April 4th, from Paris, where cholera existed, there arrived a soldier sick with diarrhœa. He was received into his parents' house where he remained three days. On the 14th he went to the Hôtel Dieu, and the same day his brother, who had come a number of times to see him, was attacked by foudroyant cholera and died in twelve hours. His wife died three days afterward. The father, who had shown some symptoms of cholerine, was attacked with cholera on the 11th, and died on the 15th. Another son of this man, seventeen years old, and a child of four years, his grandson, were attacked with cholera and got well. The father-in-law of the brother who had taken care of him and his daughter were attacked by cholera, but recovered. A child of eleven years, who was often at the house and whose parents had taken care of the same brother and his wife, was attacked on the 14th and died the following day.

Third, Can the bodies of persons dead of cholera communicate the disease? Although the evidence seems to point toward this being a possible danger, it is not a serious one in civilized countries.

'Fourth, Can cholera be transported by healthy individuals? This must be answered in the negative. The facts quoted that seem to show that this may occur, must be explained by supposing that the individuals who were believed to be entirely well were in reality sick of a choleraic diarrhœa, or else that they carried clothing or linen soiled with choleraic material. The studies of cholera during 1892–93 in Europe have shown that the cholera vibrios may be present in the dejecta of people apparently healthy, with well-formed stools, as well as in those who are suffering from a mild diarrhœa without other notable symptoms. These vibrios were virulent and presumably capable of inducing severe cholera in more susceptible individuals.

Fifth, Can cholera be transported by living animals? Animals are not susceptible to the disease. A certain number of experiments have succeeded in producing cholera in animals, but with great difficulty. There is no fact to support the supposition that animals can carry the disease, either on the skin or in the hair.

Sixth, the transportation of cholera by means of clothing, personal effects, and so on. The disease cannot be so transported unless these materials have been contaminated by cholera dejecta. This, of course, is an exceedingly important point, for if soiled, the material may be dangerous; if it is not soiled, there is no danger at all, even if it comes from cholera centres. It is of equal importance to know whether contaminated objects have been packed up or exposed to the air. A contaminated object exposed to free air for a definite time loses its power of transporting the virus. The conference of Constantinople considered that a very short time was sufficient to do away with all danger, and recent bacteriological research

has wholly confirmed this opinion. On the other hand, contaminated objects that have been packed up and kept shut out from the air retain their virulence for a greater or less length of time, as may be shown by many instances.

Seventh, Can cholera be transported by merchandise? Although merchandise imported from India, whether to Suez or directly to Europe, has never been known to transmit cholera, this method of transportation is not absolutely impossible, and many of the materials brought from India—cloths, and so on—retain in their interstices a confined air that certainly might preserve and transport for a great distance the contagion with which they may be impregnated; but although this is a possibility, it is not probable, and the conference of Constantinople unanimously accepted the absence of proofs of the transportation of cholera by merchandise, while it admitted the possibility of its being done, under certain conditions. Since that time, Zehnder, the Swiss delegate to the Vienna Conference, in 1874, cited facts in favor of the danger of rags in transporting contagion (see the report of the International Sanitary Conference of 1874, page 272). But at the conference in Rome, in 1885, Koch disputed the interpretation that had been put upon these facts.

Eighth, water is perhaps the most important agent in the spread of cholera, and evidence to this effect was obtained long before the discovery of the cholera spirilla. J. Simon brought out some facts in England which confirm this statement. At London thirteen deaths out of a thousand inhabitants occurred among those whose houses were supplied with river water in the neighborhood of the sewer. Tested at this point, the water yielded forty-six grains of solid residue to the gallon. In other houses in the city that were in the same hygienic condition, but not supplied with this water, the mortality was only three and seven-tenths in a thousand, but the water which they used had been taken from outside the city, and yielded only thirteen grains of solid residue to the gallon.

It is not improbable that the cholera vibrio can live longer in a pure water than in one containing large numbers of other micro-organisms. It has remained viable for eight hundred and seventy-eight days in a sterilized pond water, which for at least three hundred and five days contained other bacteria. During this period they retained their usual susceptibility to heat and desiccation, showing that a true spore formation of the usual kind is not necessary for prolonged viability in this species.

At Halle, Delbruck noticed that in the prison, where the epidemic had developed very largely, the wells communicated with the drains. At Brachsted the epidemic arrested itself just as soon as a suspected well was closed. Delbruck explained the less intensity of the epidemic of 1867, compared with that of 1866, by the fact that the carrying of the water had been modified. Water was furnished almost pure in 1867, while up to the autumn of 1866 the conduits carried the water from the Saale through a region where all the discharges of the city were scattered. Ballot also spoke of the influence of impure water on the spread of cholera in Holland. Snow, in England, and innumerable other writers in Europe, India, and America, lay the greatest possible stress upon impure water as the special means for the conveyance of the infective agent of cholera. (See the article on *Water*, in the present volume.)

The contamination of water played an extremely important part in the extension of cholera in Egypt in the epidemic of 1883. The Mussulman population of Egypt bathe very frequently, but they are not careful about the water that they use for drinking. At Damietta the water is exceedingly foul upon the points of the Nile from which the water-carriers fill their water-casks, and just at these places are the special spots selected for bathing. The houses along the bank discharge their foul material directly into the river, and drains carry to it discharges from other houses, and from the mosques. According to Koch, these mosques play an extremely important rôle in the spread of cholera. The German cholera commission was able at Damietta to examine a number of mosques, the description of the arrangement of which is as follows: Only that part of the mosque that is directed toward Mecca is used for prayers. At the other end is an open space, in the centre of which is a tank for bathing, and sometimes this water remains several weeks without being changed, and surrounding the basin are a series of urinals and closets. The discharges from the whole are passed into the Nile, so that it is not strange that the infected material should be transported by such a water supply.

In the "tank districts" of India the conditions appear particularly favorable for the propagation of cholera from the sick to the well. In these districts cholera is very prevalent. The region is low and the land upon which the dwellings are situated is made ground derived from the immediate neighborhood, leaving pools which constitute the "tanks." The drainage from the dwellings flows into these relatively or entirely stagnant bodies of water, which is also used for bathing and, in many cases, for drinking purposes.

The epidemic of 1884 furnished new proofs in favor of the spread of cholera through the agency of water. Messrs. Marey, Brouardel, and Thoinot especially insisted upon this point. Marey, at the sitting of the Academy of Medicine, October 14th, 1884, said: "Among the influences that can cause the spread of typhoid fever or cholera there is one that by its intensity dominates all the others—that is the contamination of public water supplies." If a number of epidemics of cholera be studied, it can be determined, in effect, that cholera easily follows watercourses; that it is especially along small watercourses that it is propagated, is most frequent and striking. In order to explain this, there are but two hypotheses that are possible.

First, brooks, torrents, or rivers flow in valleys that are often narrow and shut in, and the villages found there often can have no communication except with each other. When one is attacked, it is a perfectly simple matter that the others should be also in their turn. This explanation is very plausible; for certain cases, and some epidemics, can be explained in no other way. The great rivers, the large watercourses, along which are scattered regions attacked by cholera, serve for the propagation of this disease, like the great roads of travel, in this way only, that they are lines of communication frequented by travellers.

Second, water is certainly a propagating agent of cholera. It is the water of a torrent, a brook, or a small river, contaminated in one part of its course, that transports the disease to the inhabitants on its borders that drink of the water, and innumerable instances can be brought forward to illustrate this point also.

Proust (*loc. cit.*, p. 216) speaks of the choleraic agent having for its vehicle of transportation either the air or the water, but the evidence in favor of the air as one of the transporting agents of cholera is nothing, and the weight of scientific evidence of late years militates against such a means of transportation. Altitude seems to have but slight influence upon the development of the disease up to a certain point, although Farr (in the Registrar-General's Report on the Mortality of Cholera in England, London, 1852) has attempted to demonstrate that the mortality from cholera was in inverse proportion to the elevation. The objection to this is, that the less frequent occurrence of cholera on the most elevated points may be due to the fact that the less accessible points are more thinly inhabited.

Moisture, taken in connection with the subsoil water, is a favoring cause of the greatest importance, and observations in this direction have furnished the basis for Pettenkofer's theory of the connection of subsoil moisture with cholera.

The development of the epidemics of 1836 and of 1854 seemed to coincide with the period of greatest diminution of the subsoil moisture in Munich, and therefore the choleraic contagion with which the soil is impregnated appears to disengage itself more easily. Hirsch reached

a similar conclusion. Kreuzer, in 1855, at Vienna, and again Pettenkofer, at Munich, observed the same facts. Pettenkofer's theory differs from others, in that, putting aside the chemical composition of the earth, he attaches a special importance to its physical characteristics, its density, its porousness, etc. He considers that the condition of the subsoil of localities and of houses plays a rôle of special importance in the propagation of cholera, and upon this special cause he places the development of an epidemic, after an importation from without; and, studying almost exclusively the physical condition of the region, the compact or porous condition of the subsoil, he considers that not only the primitive earth, and the soils of the transition period, but also the secondary formations, produce immunity when they are exposed to air in the condition of rocks. On the other hand, every porous soil that is susceptible of imbibition can become easily impregnated with fluid, or with gas, and vegetable earths as well as silicious earths may form "fat," always moist, lands, throwing out continual moisture about them, favoring the diffusion of the germs of cholera. Where the soil is made up of a compact calcareous rock cholera never becomes epidemic, and a few cases observed in such situations as the result of importation, do not propagate the disease.

Pettenkofer's theory has two points that must be distinguished from each other.

First, the nature of the soil. The soil must be porous, easily permeable, and also easily impregnated by liquids and gas. This condition is a permanent one.

Second, the level of the subsoil moisture. This level being movable, the effect is variable; when subterranean waters have reached the maximum of their elevation, there is neither decomposition of organic materials nor throwing off of miasms. If the subsoil moisture descends to a lower level putrefaction begins, the miasmatic vapors are thrown off more intensely, and just at this time the epidemic reaches its greatest development. This second point of his theory, certainly an ingenious explanation of certain cases, appears to be much more hypothetical than the first, the question of the porosity of the earth.

To sum up, Pettenkofer's theory, while it scarcely has the value ascribed to it by him, certainly seems to afford a partial explanation of the propagation of cholera by means of the porosity and moisture of the earth.

Ninth, amtospheric conditions play a not very important rôle, although the influence of season is manifest, and, apparently, storms sometimes seem to aggravate considerably an epidemic.

Somatic Conditions.—Race or nationality has no influence upon the development of cholera. The special influences favoring it are those of misery, fatigue, cold, and depressing mental conditions, which, by diminishing the resisting power of the body, render it more susceptible to the influence of the epidemic. Collections of human beings, in other words, agglomeration, play a very considerable rôle in the propagation of epidemics; so also do methods of transportation. Railroads are often the means of propagation, as was the case in the instance of Altenburg, quoted above. The epidemic of 1865, in Paris, was started by a woman who left Marseilles, with a choleraic diarrhœa, and was attacked with cholera upon her arrival in Paris. Transportation by caravans does not give much chance for the spread of the disease, when the distance passed over is of great extent; in fact, a great desert is the best of all obstacles to the propagation of cholera. In ships are most often found united the conditions of crowding and confinement favorable for the development of the choleraic agent.

Proust appears to believe that these elements do not have much potency if the entire ship's company come from the same infected region—in other words, have acquired an immunity in a choleraic focus; but if the ship's company has received a partial renewal, if new persons have come on board among the acclimated passengers, cholera finds a new favorable medium for attack, and, if aiding circumstances appear, the ship may become the centre of an intense epidemic. He goes on to speak of this "law of accustoming," in what takes place in armies, the great fairs, and the pilgrimages; for when cholera is carried into these great collections, if the mass of people have not undergone the "choleraic acclimating," the explosion of the disease is rapid and the mortality considerable, but only continues for a few days, and ceases soon. The Crimean War furnishes an example of the rapidity of development and intensity of the disease among vessels free from the choleraic influence.

At the commencement of April, 1855, there reached Constantinople from France, fifteen to twenty thousand troops, made up in part of the Imperial Guard. These troops had not, during their voyage, a single case of cholera among them. They camped on the heights of Masslak, in an extremely healthy situation, and at that time there were in the city of Constantinople but very few traces of cholera. The rolls of the French military hospitals gave only fifty-three cases during March, and the roll of April 11th showed none. In the Crimea the cases of cholera were also very few, and nevertheless the troops were hardly settled at Masslak when, on the night of April 14th and 15th, cholera broke out among them, and a severe epidemic followed.

Fauvel ("Memoire lu à l'Acad. des Sciences," Paris, 1883) sums up this question of immunity in the following propositions:

"1. The ports of India that are the seat of endemic cholera are never the scene of a great epidemic.

"2. This fact relates to the general, but not absolute, immunity enjoyed by the native population of these parts.

"3. This immunity does not exist in the endemic localities for strangers who are in a condition favorable for contracting the disease. These are especially the Mussulman pilgrims who come to Bombay to embark for Mecca.

"4. The epidemics of cholera that develop in India, in the regions where the disease is not endemic, come from the places where it is endemic, and are favorable for attacking the Hindoo pilgrimages.

"5. The epidemics observed among the pilgrims to Mecca can also be traced to the localities where cholera is endemic.

"6. A severe epidemic of cholera confers upon the country or upon the locality which it has attacked a more or less complete immunity, which is more or less durable, and of which it is impossible to formulate the law for Europe, but which in India appears to last for a number of years.

"7. In the Hedjaz, and in the sparsely populated parts of Arabia, cholera has but a feeble tendency to propagate itself among the native population.

"8. The fact of the existence of a great epidemic of cholera in any country whatever is a proof that cholera is not there endemic."

To sum up, new scientific facts bear upon the question of immunity and make them clear upon a side hitherto unknown. The etiology and prophylaxis, in especial, of cholera receive from these facts new indications, and these facts also appear to be the expression of a law that includes an entirely different category of infectious diseases, which leave after them an immunity of a greater or less extent.

Period of Incubation.—The question of the period of incubation of cholera gives rise to a great deal of discussion. It appears, however, that in the immense majority of cases a period of a few days is sufficient for the incubation, and that sometimes this may require only a few hours. This fact is easy to observe if the beginning of the disease in a city or upon a ship be studied.

The Cholera Conference at Constantinople concluded as follows: "That all the facts cited in regard to a period of incubation longer than a few days are based upon cases that are not conclusive, either because the premonitory diarrhœa was comprised in the period of incubation, or because the infection could have occurred after the departure from the infected locality." The following is an instance:

On November 3d, 1848, upon the ship *Scanton* there were two hundred and eighty-nine emigrants for New Orleans, and the cholera did not break out on board until November 25th—that is to say, the twenty-third day of the voyage—and occasioned thirteen deaths. A certain number of these emigrants came from points in Germany where the cholera existed. This long period of incubation can be explained upon two hypotheses: either the passengers had with them clothing soiled with choleraic materials, which, placed in a confined air, could transmit cholera; or certain of the individuals embarked might have been affected at the time of their embarkation with a diarrhœa that might later have developed into true cholera. The duration of this premonitory diarrhœa has been much discussed, and in general it has been concluded that it does not last more than three days, and when it does pass this period, it is rarely prolonged beyond a week, and that therefore an individual isolated from all sources of contamination, and in whom the diarrhœa should be prolonged more than eight days after this isolation without presenting any characteristics of cholera, could be considered non-choleraic. But Griesinger among others dissents from this opinion, and declares that the period of incubation of cholera may be much longer. A bacteriological examination furnishes the only method of settling the question.

The experience of those who carefully studied the epidemic in Hamburg in 1892–93 points to an incubation of not less than twenty-four hours. After this period there may be a diarrhœa which attracts little attention, but which is in reality the first stage of the disease. In other cases the onset of symptoms may be very sudden, leading to collapse and death within a few hours. It has been noted that in the early days of an epidemic the spirillum develops more slowly in artificial media than is the case later in the course of the epidemic.

Description of the Disease.—The clinical manifestations associated with the presence of the cholera vibrio in the intestinal contents are so various that it is impossible to give a single clinical picture of Asiatic cholera. During epidemics of the disease this micro-organism has frequently been isolated from the fæces of people presenting no evidence of any disturbance in health. In other cases its presence is associated with symptoms of the most marked character, followed by a speedily fatal issue. These facts by no means throw doubt upon the etiological significance of the cholera vibrio; for similar observations are well known in other infectious diseases, such as diphtheria, typhoid fever, and even infections with pyogenic micro-organisms.

Cases in which the cholera vibrio is present in the digestive tract without being associated with symptoms are of great sanitary importance, because this very absence of all manifestations of disease renders the spread of the infection from place to place very difficult of control or detection. It is also important to the individual himself. There are cases on record in which people in apparently perfect health have left regions where cholera was epidemic, have remained for a time free of any signs of ill health, and then, as the result of some dietary indiscretion, have suddenly succumbed to an attack of severe cholera, with the vibrios in the alvine discharges. It appears evident that in such cases the cholera vibrios in the intestine are virulent, but that the resistance of the individual was so great as to prevent the usual effects of infection until some additional factor created a susceptibility. It is not possible to state the frequency of such latent infections in times of epidemic cholera, but where the spread of the disease takes place through a contaminated water supply it is reasonable to suppose that they must be more frequent than could be indicated by any statistics as yet in existence. Rumpf, in his studies of the epidemic in Hamburg in 1892–93, reports that cholera vibrios were found in the fæces of 62 individuals during the small after-epidemic of 1893, and that of these 19 failed to show signs of any great constitutional disturbance. These cases were studied because they had been closely associated with cases of pronounced cholera in the city or upon vessels in the port. On the other hand, between February 23d and June 1st, 1893, 70 cases of diarrhœa were investigated to learn of the presence of cholera vibrios in the discharges, with negative results.

Leaving out of further consideration these important latent infections, we may divide cases of cholera into three groups, according to the severity of the clinical manifestations: First, choleraic diarrhœa, in which the symptoms present little beyond a marked looseness of the bowels; second, cholerine, characterized by vomiting and considerable constitutional disturbance as well as diarrhœa with rice-water discharges; and, third, algid or asphyctic cholera or cholera gravis, which has hitherto served as the type of the disease.

These terms are not used to denote nosological entities, but merely to furnish concise expressions for clinical differences dependent upon variations in the relations between the virulence of the infection and the susceptibility of the patient. In individual cases the less severe forms of the disease may pass into the graver types, where conditions arise which modify these relations. In many epidemics the milder types occur most frequently early in the history of the epidemic, to be succeeded by a larger percentage of severe cases at the height of the epidemic, which are in turn followed by a preponderance of the milder cases as the epidemic draws to a close. These clinical observations harmonize with the experience that cultures in artificial media grow less rapidly early and late in an epidemic than at its height.

Choleraic Diarrhœa.—In the milder cases the stools are feculent or bile-stained and watery, are unaccompanied by much pain, and differ considerably in frequency in different cases. The symptoms usually first appear at night and are accompanied by some flatulence. The general health may remain good. In severer cases the stools are more numerous; the appetite is lost; the tongue becomes coated, and there is a feeling of gastric depression. The amount of urine is decreased. The patient becomes restless and suffers from headache. Dragging pains in the calves may be troublesome. These symptoms last a few days, and in favorable cases then subside. The course of the affection depends largely upon collateral circumstances. Indiscretions in diet, overfatigue or imprudence of any kind exert an unfavorable influence upon the patient, and in many cases this choleraic diarrhœa passes into the severer forms of cholera. Although the cholera vibrios are regularly found in the discharges, the latter do not acquire the rice-water character typical of the severer forms of the disease.

The affection may prove fatal in people of diminished resistance; in the young or aged death being the result of exhaustion; but recovery is the rule.

Cholerine.—Sometimes this type of cholera is preceded by the form just described, but more often the first symptoms noted are general malaise, loss of appetite, and nausea. The stools then become more frequent. They are at first feculent, but soon become more liquid and then assume the "rice-water" character of those in severer cases of cholera. These discharges consist of a serous fluid, rendered turbid by large quantities of desquamated intestinal epithelia, and frequently tinged more or less pinkish by red blood corpuscles. When examined microscopically the spirilla may frequently be seen in great numbers, but in many cases they cannot be made out as such, but appear as granules of various shapes. In addition to the symptoms mentioned above, vomiting comes on early in this form of the disease. After the stomach is emptied of food, the vomitus is a thin fluid containing some bile, or it may be colorless. Pain in the epigastrium, headache, and thirst appear as the disease progresses. The quantity of urine is reduced and albuminuria appears. The skin is cool and the volume of the pulse diminished.

Cholerine may pass into algid cholera, or the symptoms may gradually subside and recovery follow; but not infrequently convalescence is delayed by a long period of debility and mental hebetude, resembling the typhoidal stage of algid cholera.

Cholera Gravis; Algid or Asphyctic Cholera.—In this form, which has usually been regarded as the typical manifestation of the disease, the attack may suddenly develop, its onset being marked by great uneasiness, repeated discharges from the bowels, followed by syncope. This attack may overtake the victim while walking on the street in apparently good health. It is often preceded by a state of vague suffering, rapid prostration, deep colicky pains, anorexia, sometimes a diarrhœa, profuse sweats, disturbance of the senses, and more or less retardation of the pulse. After the development of the disease the symptoms follow each other in such a way as to allow of a division into two distinct periods.

First Period.—This is marked by an increase in the number of dejections and acts of vomiting; a flux is established which is at first serous or slightly bilious, and afterward becomes "choleraic." This term is used to designate those characteristic discharges of cholera which are liquid, whitish, grumous, sometimes resembling unclarified whey, sometimes a decoction of rice or oatmeal, and sometimes thickened meal, and nearly clear, which emit an insipid spermatic odor, and sometimes present traces of blood or bile. These evacuations are rarely absent, often continuing to the termination of the disease. Burning thirst, pain in the epigastrium, and prolonged hiccough are usual accompaniments. Intense cramps of the limbs occur, particularly in the calves of the legs; the muscles are often in a state of tonic contraction. Spasmodic movements, as involuntary flexion and extension of the fingers and toes, may often be seen. The pulse is very feeble, often imperceptible. The features are altered, trembling and great agitation come on, the pulse becomes suppressed; bluish spots appear, first upon the extremities; the skin becomes blue or black almost everywhere; the nails are livid and almost black, the fingers wrinkled, and the genital organs retracted. The volume of the body diminishes rapidly and perceptibly; the eyes sink in and are dull, with a bluish circle surrounding them; the conjunctiva fades, respiration is slow and feeble, the breath cold, and the pulse is reduced to a mere oscillation. The secretions are arrested, especially the urine, the voice is reduced to a whisper, the nose is cold and—rarely—gangrenous, the cornea is flattened and puckered; spots of blood appear on the sclerotic, viscid sweat on the face and limbs; the intellect becomes obscured, respiration is embarrassed, hiccough commences, and death follows, in the midst of an apparent calm. This is called the *cold*, *livid*, or *asphyctic* period. When patients escape death in this stage they enter upon the

Second Period.—In this the coldness ceases to increase, warmth returns, the pulse improves and gradually becomes febrile, the face regains color, the eye becomes animated, and a general reaction occurs.

If recovery is to be easy and rapid, vomiting becomes less frequent, the diarrhœa remains, but the discharges no longer present the appearance peculiar to the disease; the secretion of urine returns, nausea, thirst, and pains in the stomach cease to be felt, the pulse becomes regular, and convalescence begins.

If reaction is incomplete, the cold stage returns with renewed severtiy, or, on the other hand, if reaction be too severe, such accidents may occur as apoplexies, spasms, convulsions, local congestions and inflammations, and occasionally latent pneumonia. Stupor is sometimes present, with some of the signs of the last stage of typhoid fever. Swelling of the parotid glands and various skin affections, as roseola, urticaria, erythema, erysipelas, etc., may appear toward the close of the disease.

The average duration is from one to three days, but sometimes death occurs in less than six hours, and is occasionally delayed a long time—in one case for fifty days.

Complications and Secondary Affections.—Complications are rare, and apparently accidental, but secondary affections, either direct results of the cholera or due to increased susceptibility to infection or to debility, are common.

Course, Duration, and Termination.—If death does not occur during the algid stage, a peculiar transformation in the disease takes place and *reaction* sets in. This reaction varies in different cases, being slow and tedious in some, and abrupt and rapid in others; its course is not essentially modified by any antecedent disease, even those occurring as complications.

In the vast majority of cases cholera runs its course with great rapidity, the greater number of attacks lasting from eighteen to twenty-four hours, the shortest from one to six hours, and the longest from fifteen to twenty days. Its duration is the shortest at the height of an epidemic.

The termination of epidemic cholera may be favorable, the progress of recovery varying widely in different cases; it may be complete in a few hours even, and the patient may return to his ordinary occupation; on the other hand, it may be delayed until after a long and perilous struggle against complications and secondary affections. There may remain a general debility such as is not often seen after any other disease; the emaciated features, languishing expression, capricious appetite, obstinate gastralgia, colic, wakefulness, tendency to coldness, partial or general, and intellectual and moral dejection persist for a long time. An attack has been known to change the whole constitution and temperament of a patient. One attack appears to furnish no immunity against another, and relapses are always to be feared.

Symptoms in Detail.—Besides this general account of the disease the symptoms should be briefly discussed in the order of their occurrence.

Precursory Phenomena.—An attack is often preceded by initiatory uneasiness, which should attract attention; such are languor, pallor, anxious expression, sunken features, weight in the stomach, and movements of the intestines. Then vertigo follows, with abdominal pain, dimness of vision, and difficulty of hearing; the eyes become more brilliant than ordinary, like those of a drunken man. Sometimes circulatory disturbances are the first phenomena of the disease, marked by bluish circles around the eyes. In other cases, the progress of the preliminary symptoms differs—there are diminution of appetite for several days, general disagreeable sensations, and frequent alvine dejections, without pain, which are yellowish, more and more fluid, and, finally, become almost like water. A diarrhœa like this may occur without any other symptoms and develop into a severe case of cholera. Lastly, the disease may come on suddenly, and without warning overwhelm the victim with its full force—this often occurring at night.

Diarrhœa.—This is most frequently the mark of the onset of the disease, and when it is so, the stools become at once more and more frequent. Fifteen, twenty, or more dejections in twenty-four hours are usual, and in some cases (these are fatal) the evacuations occur in an almost continuous and involuntary jet. They are often accompanied by colic, borborygmi, and gurgling, either spontaneous or excited by pressure upon the abdomen. They are at first made up of bilious, fæcal, or sero-mucous matter, but soon assume the characteristic appearance, viz., that of a whitish flocculent fluid such as has already been described. A large flocculent sediment is deposited from this fluid, a part of it looking remarkably like cooked rice. The fluid is blood-serum, and the sediment is made up of the epithelial lining of the intestines and of mucus. Sometimes the evacuations are tinged with blood-coloring matter, giving them the appearance of the lees of wine, or they may be of a deep brownish color from the same cause. The frequency of the dejections is not always increased with the progress of the disease, they are occasionally completely arrested during the cold period, and death may occur without their beginning again; on the other hand, they may return with increased violence. In those cases in which the acute attack is followed by a prolonged period of depression, during which the patient presents the typhoid state, the choleraic discharges give place to loose, diarrhœal evacuations having a fæcal odor. These may be frequent and persist for a number of days, gradually diminishing as convalescence advances;

but the typhoid condition is always favorable to the development of dangerous complications, and cases of cholera which take this form are by no means favorable. The abundance of the renal secretion is considered a valuable prognostic sign. After recovery obstinate constipation may occur.

Vomiting.—Nausea and vomiting, sometimes almost constant, occur from the very beginning of the disease. The vomitus is poured out by an almost constant effort; it does not differ in character from the dejecta, except that it is sometimes more limpid, and is sometimes slightly tinged with bile. It is very rare that vomiting persists to the second period of the disease, but the ingestion of the smallest quantity of fluid may excite it with great violence. It often alternates or coincides with a very troublesome hiccough.

Abdominal Pain.—This often precedes the vomiting and choleraic diarrhœa. It is griping, and of the most intense character, situated in the region of the epigastrium, or over the entire abdomen. A doughy sensation is communicated to the hand upon pressure, and percussion gives, usually, an almost universal dull or flat note.

Anorexia; Thirst; Tongue.—Loss of appetite is complete, and corresponds in point of time with a burning and inextinguishable thirst. The throat and mouth are parched, the tongue is frequently clean, commonly large, pale, moist, cold, very rarely dry, and occasionally covered with a yellowish coat. This condition is peculiar to the first period; it varies, later on, with the degree of reaction, or with the nature of the complications and secondary affections.

Urine.—Upon the first appearance of the gastro-intestinal evacuations the urine becomes scanty, and is frequently completely suppressed; exceptional cases are reported in which it remains normal throughout. Emission is involuntary. Sometimes, after suppression, it reappears about the middle of the cold stage; being again suppressed for the remainder of the disease. The desire to urinate remains, although the power may be lost; the secretion and flow are generally re-established during the period of reaction. There are no observations pointing to the occurrence of renal disease. The urine is especially rich in indican and other ethereal sulphates. Ammonium salts are also increased and aceto-acetic acid may be present in considerable quantities. These changes in the urine are attributable to the ready absorption of putrefactive products from the intestinal contents, due in part at least to the loss of the epithelial lining of the bowel, and to the reduction of oxidative processes within the body.

Cramps.—Violent and prolonged cramps, beginning with the first diarrhœa, in the muscles of the legs and extending to the abdomen, arms, and even to the face, are among the most characteristic, and at the same time the most terrible, symptoms of cholera. They sometimes persist throughout an attack, and even after a cure, and muscular contractions have even been observed after life was extinct. During an epidemic cramps have been observed without any other symptoms. It has been suggested (Weir Mitchell: "Injuries of Nerves," p. 52, ed. 1872) that they are caused by the loss of water from the body, and the consequent "drying" and irritability of the nervous system, a phenomenon analogous to the violent contractions of a frog's leg when the sciatic nerve is exposed and allowed to dry in the air.

Headache; Derangement of the Senses.—Weight in the head, with giddiness and vertigo, occurs during the invasion; cephalalgia, often very severe, appears during reaction; it is generally heavy, and more marked in the frontal regions; at the same time occur ringing and buzzing in the ears. The sight is generally affected during the whole course of the disease; it is blurred, double, or perverted, so that the patient sees objects colored blue, or alternately black and red; it is occasionally completely extinct. The touch and general sensibility are much blunted.

Intellectual Faculties.—These are generally unaltered, although the power of expression may be impaired. It is only in certain modes of reaction in the second stage, and in certain complications, that stupor and, more rarely, delirium occur.

Strength.—There is in all cases almost entire loss of strength, the least displacement of the limbs being unbearable. Most patients, either stretched on the back or with the limbs closely drawn up, remain in a state of complete immobility through fear of fatigue. Transient faintness appears in some cases.

Voice.—It is characteristic; changing very rapidly from a state of feebleness at the commencement of the disease to a rough and whistling tone. It occasionally becomes entirely extinct, but in some cases retains strength enough for loud cries. It gradually returns to its normal condition as the disease lessens in intensity and recovery progresses.

Respiration is ordinarily very difficult, the frequency varying from ten to fifty-two per minute. This does not depend upon any altered condition of the lungs as revealed by physical examination, but seems to be in some way connected with the presence of less than the normal amount of carbonic acid in the expired air.

Circulation.—The circulation is very gravely affected. The pulse becomes more and more feeble, and disappears entirely at the height of the cold period; it is always more frequent than in health. The blood moves slowly and will not flow from a vein or an artery of small size. This sort of stagnation aids in producing the bluish hue peculiar to the cold stage. This bluish hue makes its appearance first in the extremities, in the genital organs, and in the face. It is especially observable in patients who are plethoric and of florid complexion. It diminishes and often disappears during reaction, and sometimes does not occur at all. It may go so far as to produce gangrene, as has been observed in the nose, tongue, and sexual organs.

Temperature.—The temperature is seemingly reduced; the expired air being only 25° to 27° C. (77° to 80.6° F.). This reduction in temperature is confined to the surface, however, the internal temperature being higher than in the highest fever (Guterbock, *Virch. Arch.*, xxxviii., p. 30).

Appearance.—The aspect is characteristic; the face is contracted, the brow wrinkled, the cheeks are hollow, the lips thin and pressed in upon the teeth, the complexion becomes livid and bluish, the eyes more and more sunken, and surrounded by a dark circle. Expression is lost by degrees, and death seems to have occurred while life is still present. The eye is dim, its surface wrinkled, sunken, and sometimes dry, the globe is left exposed by the lids, and the conjunctiva becomes injected and covered with spots of blood. Even if recovery takes place, the normal aspect of the face returns very slowly.

Complications. Secondary Affections.—*Complications* are rare and apparently accidental; among them peritonitis, jaundice, gangrene, œdema of the lungs, erysipelas of the face, abscesses, ulceration of the eyelids, and aphthæ may be mentioned as of occasional occurrence.

Secondary affections are, however, very common. They may consist of gastro-intestinal inflammations, immediate, or after some days of convalescence, or of affections of the respiratory organs. In other cases persons who have apparently escaped the accidents of cholera have a secondary fever, described as of a typhoidal type, dry skin, tension and tenderness in the epigastrium, jactitation, dry tongue, bilious stools, and chills. Various skin eruptions occur, and temporary albuminuria has been observed following an attack of cholera. The most grave of the secondary affections, however, are those which affect the nervous system. The cerebral congestions during reaction are, in some cases, followed by a typical meningitis with trismus. Rayer's "État cérébral cholérique" includes a group of phenomena distinct from those of meningitis, which supervenes upon the cold stage; the skin is cold, the pulse feeble, the head heavy, the countenance stupid, and sometimes the cholera tint remains. Other affections are

a sort of non-febrile delirium, lasting for two or three days, and the spasmodic contractions of the forearm which occur during convalescence. True intermittent febrile attacks, with initial chills, occurring every day during reaction, have also been observed. All these affections are, for the most part, more rapid than when occurring in the individual previously healthy.

Pathology.—Until more is known of the exact nature of the toxic substances which can be elaborated by the cholera spirillum, when present in the human intestine, no very exact statements of the pathology of the disease can be given. It is evident that an irritation of the intestinal mucosa, with more or less damage to the histological structures, is caused by the spirillum or its products, and that in pronounced cases a very abundant transudate of fluid follows. Many of the symptoms of the disease, especially in the algid stage, are due to the consequent loss of fluid on the part of the blood and tissues of the body. In addition to this loss of fluid there are reflex nervous influences upon the heart and perhaps other parts of the body, due to the lesions in the intestine, and toxic substances absorbed from the intestinal contents probably act upon the cells of the viscera. To these factors, *i.e.*, loss of fluid, nervous reflexes and toxæmia, which account for the symptoms of the disease, may be added an increased susceptibility to secondary infections.

Pathological Anatomy.—The alterations of the internal organs in a case of death from cholera bear little relation to the violence of the disease. The appearances are about as follows: Emaciation is general, and there is marked lividity of the lips and nostrils. Rigor mortis is not rare before the warmth of the body has wholly departed and is very marked and prolonged. The peritoneal surface is sticky and covered with a viscid exudation (present in 91.6 per cent. of 530 cases); the vessels of the mesentery are engorged with blood. The calibre of the intestinal canal is more often increased than diminished, and always contains some fluid choleraic matter. The fluid is blood serum, containing a variable number of red corpuscles, and the thicker material found in it is made up of intestinal epithelial cells and mucus. The intestinal mucous membrane is usually normal in thickness, but is generally denuded of epithelium. The villi are swollen, giving the surface a velvety appearance, and Peyer's patches and the solitary follicles are much enlarged. The glands of the stomach and of the duodenum are enlarged, and the surface is largely denuded of epithelium. There are no special lesions of the other organs. The liver is rarely enlarged, is the seat of moderate cloudy swelling, and is usually congested with dark thick blood. The gall-bladder generally contains bile, which is at first thicker than normal, but subsequently becomes more abundant and pale. The biliary duct is not obstructed. The pancreas presents no marked alteration. The spleen in rapid cases is small, hard, and wrinkled upon its surface, of a deep red color on section, and sometimes dotted with ecchymoses; in slow cases it may be slightly enlarged and less deep red in color. The blood is thicker than normal, coagulates slowly, and the separation into clot and serum is very incomplete. The corpuscles are not altered in shape, but there is a remarkable diminution in the proportion of water and neutral salts, and a decrease in the amount of fibrin and albumin. The heart is usually soft and flabby, the muscle degenerated, with ecchymoses in the pericardium. The left side is apt to be empty and contracted, the right distended with dark, thick blood. The arteries are, in general, nearly empty, the veins distended with blood. The pleuræ are very frequently coated with a glutinous, stringy substance, and ecchymoses often appear in the subpleural cellular tissue. The lungs are usually healthy, but presenting engorgements at the posterior portions; or they may contain pneumonic areas or abscesses due to inhaled vomitus. The bronchi are much congested, and may contain a white, stringy mucus, analogous to that found lining the intestinal canal. The condition of the brain and spinal cord, together with their appendages, is merely that of congestion without special lesion, although it has been declared that there is a sensible increase in their consistence. The ganglionic system presents no change worthy of notice. The muscles are often engorged with blood, and a very marked reddish-brown discoloration of the bones and of the teeth has been noticed in those dying of asphyxia. Renal congestion is the marked alteration in connection with the genito-urinary tract, and the straight tubules are often completely stripped of their epithelium. The epithelium of the convoluted tubules suffers marked parenchymatous degeneration, even in cases of short duration. In those dying in the cold stage the bladder is empty and firmly contracted. The uterus usually shows a hemorrhagic endometritis, and abortion is the rule in pregnant women.

Description of the Spirillum of Cholera.—Asiatic cholera is without doubt due to a special organism—the so-called "comma bacillus" of Koch—this name being a misnomer, for the bacterium is not a bacillus, but a spirillum.

The parasitic nature of the disease was suspected for a long time. A number of observers had noted the presence, in the cells, of bacteria answering the description of this special one, but it was not until the advance in methods of observation had progressed a long way that it was possible to isolate the organism, and study it under artificial conditions in such a manner as to obtain the evidence necessary to connect it with the process as a causal factor. It was in the year 1883 that Koch first discovered and described the spirillum of Asiatic cholera, which he first found during his investigation in Egypt during the epidemic there, and studied further during the following winter in India.

The organism occurs especially in the small intestine, is generally wholly confined to the contents of the intestine and the glandular culs-de-sac, but is occasionally found in the intestinal walls. It is exceptional to find it in any other part of the body, and it is not strange that investigations undertaken with the idea that cholera was a generalized disease were not productive of results. The bacterium is found in large quantities in the dejecta, and sometimes—in fact not infrequently—in almost a pure culture.

In the intestines and in the dejecta it presents the appearance of a short, thick rod, slightly curved in the long diameter, hardly half as long, but considerably thicker than the bacillus of tuberculosis. It usually occurs in this situation singly, but not infrequently it is arranged in pairs, with the curves opposed to each other, and thus recalling the shape of the letter "**S.**" There are many exceptions to this rule, and a simple microscopical examination of the dejecta does not suffice to establish a diagnosis of Asiatic cholera, or to exclude such a diagnosis. Sometimes no curved, **S**-shaped, or spirilliform organisms are seen, but the preparation contains numerous granules of various shapes. If, however, plate cultures are made from these discharges, they may yield practically pure cultures of the cholera spirillum. Even when very small quantities of the dejecta are used, the colonies may crowd the plates. Under cultivation in bouillon the organism appears longer and thinner, and there are many true spirilla to be seen in the preparations made from such a culture. (See Plate LIX.)

A characteristic that is of especial interest is its extreme motility, which has been demonstrated by Löffler to be due to a fine cilium or two, occasionally three cilia, which are longer than the bacteria, placed at one end of the organism. Shortly before division, both ends possess cilia. After prolonged artificial cultivation the motility is reduced in activity.

Shape and motility are not, however, sufficient to differentiate this bacterium from others with similar characteristics—and there are many that possess such—but the method of development upon the various culture media is entirely characteristic, and, as shown by Koch, is all that is necessary for separating this one in particular from the others that resemble it. It liquefies gelatin, but it does this slowly, and at the same time a certain part of this liquefied portion evaporates, and as a result

there is a special appearance of the culture that is shared by only a few other spirilla. At the upper portion of the gelatin there is a round cavity full of air, and as the surrounding gelatin has remained solid, the appearance is that of a bubble of air in the midst of the upper part of the gelatin and above the liquefied part. The appearance is wholly different when the organism found by Finkler is put under the same conditions, and equally so with the cheese spirillum of Deneke. The spirillum of Metschnikoff grows in very similar fashion in stab cultures in gelatin, and there have been isolated from water and other sources spirilla which cannot be distinguished from the cholera vibrio in this culture medium.

Morphology.—Slightly curved rods, with rounded ends, from 0.8 μ to 3 μ long, and about 0.3 μ to 0.5 μ broad. They are usually but slightly curved, like a comma, but are occasionally in the form of a half-circle, or two united rods curved in opposite directions, forming an **S** shaped figure. Under certain circumstances these curved rods may develop into long spiral filaments, and in hanging-drop cultures the **S**-shaped figures may also be seen to form the commencement of a spiral. In stained preparations the spiral character of the long filaments is often obliterated, or nearly so. When development is very rapid, the short curved rods, or **S**-shaped spirals, only are seen, but in hanging-drop cultures, or in media in which the development is retarded by an unfavorable temperature, the presence of a little alcohol, and so on, the long spiral filaments are quite numerous, and it is quite generally agreed that the so-called comma bacillus is really only a fragment of a true spirillum.

By Löffler's method of staining, the rods may be seen to have from one to three terminal flagella. In old cultures the bacilli frequently lose their characteristic form, and become variously swollen and distorted. Hueppe has described the appearance in the course of the spiral filaments, of spherical bodies which he believes to be reproductive elements, the so-called arthrospores. These bodies are not functionally spores; for cultures containing them are no more resistant than those which contain spirilla without these bodies. The cholera bacillus stains with the usual aniline colors, but not so quickly as many other bacteria. It is best stained by a watery solution of fuchsin. It will not stain by Gram's method. Sections may be stained by Löffler's methylene blue.

Biological Characters.—It is an aërobic, facultative anaërobic, liquefying, motile spirillum, grows in the usual culture media at the room temperature, more rapidly in the incubator, does not develop above 42° C. or below 14° C., does not form endogenous spores. In gelatin plate cultures, at 22° C., at the end of twenty-four hours small white colonies may be perceived in the depth of the gelatin. These grow toward the surface, and cause liquefaction of the gelatin in the form of a funnel that gradually increases in depth, and at the bottom of which is seen the colony, in the form of a small white mass. As a result of this, the plates on the second or third day appear to be perforated with numerous small holes; later, the gelatin is entirely liquefied. Under a low power, the young colonies, before liquefaction has commenced, present a somewhat characteristic appearance. They are of a white, or pale yellow color, with a more or less irregular outline, the margins being rough and uneven; the texture is coarsely granular, and the surface looks as if it was covered with little fragments of broken glass, while the colony has a shining appearance. When liquefaction commences, an ill-defined halo is first seen to surround the granular colony, which by transmitted light has a peculiar roseate hue.

In gelatin needle cultures development occurs all along the line of inoculation, but liquefaction of the gelatin occurs at first only near the surface. On the second day, at 20° C., a short funnel is formed that has a comparatively narrow mouth, the upper portion containing air; just below this is the whitish viscid mass of the growth. At the end of from four to six days, the funnel, having increased in depth and diameter, may reach the walls of the test tube. In from eight to fourteen days the upper two-thirds of the gelatin is completely liquefied. Owing to the slight liquefaction occurring along the line of growth the first three or four days, the central mass that has formed along the line of inoculation settles down as a curved or irregularly bent yellowish-white thread, in the lower part of a slender tube filled with liquefied gelatin, the upper part of which widens out, and is continuous with the funnel above. (See Fig. 5 of Plate LIX.)

On the surface of nutrient agar a moist, shining, white layer is formed along the line of inoculation. Blood serum is slowly liquefied. On potato in the incubator, a rather thin semitransparent brown, or grayish-brown layer is developed.

In nutrient bouillon the development is abundant and rapid, especially in the incubator. The fluid is only slightly clouded, but the spirilla accumulate at the surface, forming a wrinkled membranous layer.

Sterilized milk is also a favorable culture medium. The milk, however, is not visibly altered by the growth of the bacilli.

In general this organism grows in any fluid containing a small quantity of organic material and having a slightly alkaline reaction. An acid reaction of the culture medium prevents its development as a rule, but it has the power of gradually accommodating itself to the presence of vegetable acids, and grows upon potatoes (in the incubator only) which have a slightly acid reaction. Abundant development occurs in bouillon which has been diluted with eight or ten parts of water, and the experiments of Wolffhügel and Riedel show that it also multiplies to some extent in sterilized river or well water, and that it preserves its vitality in such water for several months, but in milk or water containing other bacteria it dies out in a few days. This organism is destroyed, in recent cultures, in nutrient gelatin at 52° C., as determined by Sternberg, the time of exposure being four minutes. A few colonies only develop after exposure to a temperature of 50° C. for ten minutes. In Kitasato's experiments ten or even fifteen minutes' exposure to a temperature of 55° C. was not always successful in destroying the vitality of the spirilla, although in certain cultures exposure to 50° C. for fifteen minutes was successful. The low resisting power to heat, desiccation, and chemical agents, indicates that this organism does not form spores, and most bacteriologists agree that this is the case.

Hueppe has described a mode of spore formation which is different from that occurring among the bacilli, that is, the formation of so-called arthrospores. These are said to be developed in the course of the spiral threads, not as endogenous, refractive spores, but as spherical bodies with a somewhat greater diameter and somewhat more refractive; but this method of spore formation has not been observed by others who have investigated the question, and cannot be considered established.

The test for the presence of the cholera spirilla originated by Bujwid and by Dunham consists in the reddish-violet color produced in the bouillon cultures containing peptone, or in cultures in nutrient gelatin when a small quantity (five to ten per cent.) of sulphuric acid is added to the cultures. According to Fraenkel this test serves to distinguish it from the ordinary bacteria of the intestine, and from the Finkler-Prior spirillum, but not from Metschnikoff's spirillum. The reaction is shown by bouillon cultures which have been in the incubator for ten or twelve hours, and by gelatin cultures in which liquefaction has occurred. The sulphuric acid should be quite pure. The color quickly appears, and is reddish-violet or purplish-red. According to Salkowski, the red color is due to the well-known indol reaction, which in cultures of the cholera spirillum is exceptionally intense and rapid in its development.

The most satisfactory method for obtaining the "cholera-red" reaction—as we have had lately abundant opportunity to verify—is that of Beyerinck ("Cat. f. Bact. ü. Parasit.," Bd. xii., S. 715) in which cultures are made in filtered neutralized one-half-per-cent. solution of commercial peptone, at 37° C. After twelve to twenty-

EXPLANATION OF
PLATE LIX.

EXPLANATION OF PLATE LIX.

FIG. 1.—Mucus from the Intestine of a Cholera Patient. Cover glass preparation, stained with gentian violet. Magnified 800 diameters. (Fraenkel.)

FIG. 2.—Colony of Cholera Bacilli in Gelatin, after the Lapse of Seventy-two Hours. Magnified 75 diameters. (Plagge.)

FIG. 3.—Colony of Cholera Bacilli in Gelatin, after the Lapse of Seventy-two Hours. Magnified 170 diameters. (Koch.)

FIG. 4.—Cholera Bacilli from a Bouillon Culture at the Expiration of Twenty-four Hours. Cover-glass preparation stained with fuchsin. Magnified 1,000 diameters. (Koch.)

FIG. 5.—Needle Cultures of Cholera Bacilli in Nutrient Gelatin, at the expiration of one day, three days, four days, five days, seven days, and ten days, respectively. (From Koch and Gaffky: "Bericht über die Thätigkeit der zur Erforschung der Cholera im Jahre 1883 nach Egypten und Indien entsandten Commission," Berlin, 1887.)

FIG 1.

FIG 2.

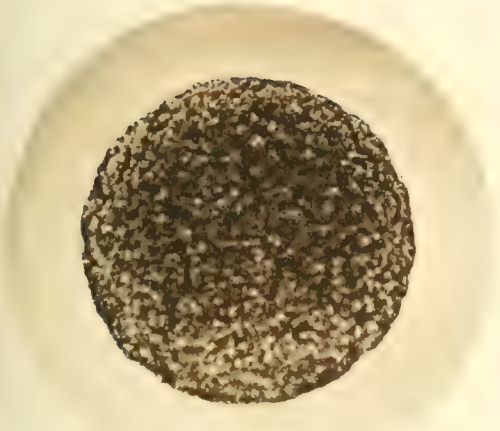

FIG.3.

FIG.4.

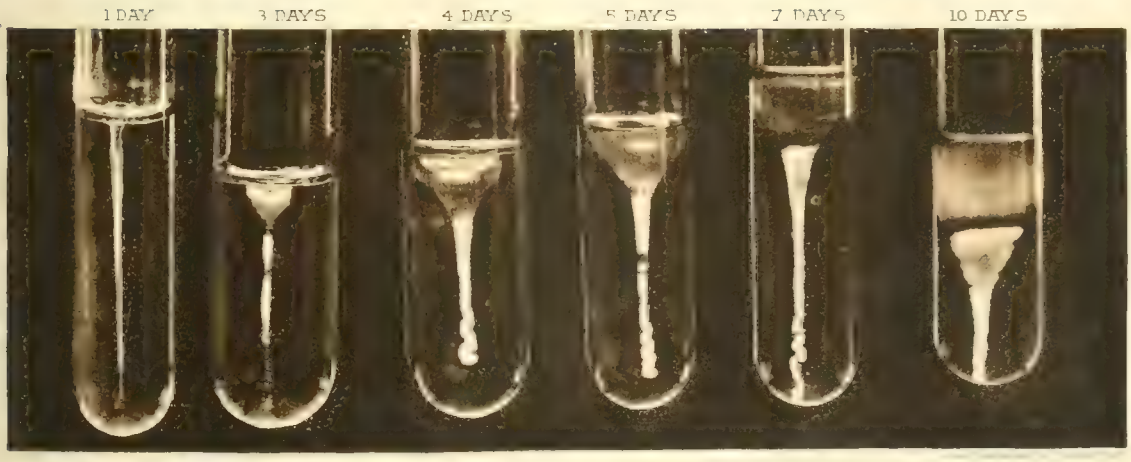

FIG.5.

ASIATIC CHOLERA.

CULTURES AND STAINED COVER-GLASS PREPARATIONS
(AFTER KOCH AND GAFFKY)

four hours the cultures are cooled, and from two to five drops of chemically pure sulphuric acid are added. If the spirillum be present, a very marked and beautiful rose-violet color is produced in the course of a few moments. In peptone-water cultures this indol reaction is perceptible as soon as the faintest clouding of the medium can be observed. Four to six hours' incubation at 37° C. may suffice.

A test which is said to distinguish cultures of the cholera spirillum from the spirillum of Deneke and that of Finkler-Prior has been suggested by Cahen. This consists in adding a solution of litmus to the bouillon, and in making the cultures at 37° C. The cholera cultures show on the following day a decoloration which does not occur at this temperature with the other spirilla named. For determining as promptly as possible whether certain suspected excreta contain the cholera spirilla, a little of the material may be used to inoculate greatly diluted bouillon, or a one-per-cent. peptone, one-half-per-cent. salt solution, gelatin plates being made at the same time. At the end of ten or twelve hours the cholera spirilla, if present, will already have formed a characteristic wrinkled film upon the surface of the bouillon. A little of this should be used to start a new culture in bouillon, and a series of gelatin plates made from it, after which the indol test may be applied. In the peptone solution mentioned above, the cholera spirilla seek the surface of the medium, and if cultivated at 37° C. a little of the material may be taken with a loop from the surface at the expiration of three hours and used for plate cultures or for examination in the hanging drop. The result of this, in connection with the morphology of the micro-organisms forming the film, and the character of growth in the gelatin plates, will establish the diagnosis, if the cholera spirillum is present in considerable numbers; if but few are present in the original material it may be necessary to make two or more series of plates and bouillon cultures before a pure culture can be obtained, and a positive diagnosis made. These tests will suffice for the purpose in times of epidemic cholera, but when there is doubt concerning the existence of cholera in the region, more rigorous identification is desirable. The virulence of the cultures may be tested on guinea-pigs and the agglutinative test with the serum of immunized animals applied.

Pfeiffer has shown that recent aërobic cultures of the cholera spirillum contain a specific toxic substance fatal to guinea-pigs in extremely small doses. This substance stands in close relation with the bacterial cells, and is perhaps an integral part of the same.

The spirilla may be killed by chloroform, by thymol, or by desiccation without apparent injury to the toxic character of this material. It is destroyed, however, by absolute alcohol, by concentrated solutions of neutral salts, and by the boiling temperature, and secondary products are formed which have a similar physiological action, but are from ten to twenty times less potent.

Similar toxic substances were obtained by Pfeiffer from cultures of the Finkler-Prior spirilla, and from the spirilla of Metschnikoff.

The spirillum is not found in the blood, nor in the various organs of individuals dead of cholera, but is always found in the discharges during life, and in the contents of the intestines examined immediately after death, frequently in almost a pure culture in the colorless rice-water discharges. They may persist in the discharges for twenty-three or more days, but usually disappear from the ninth to the twelfth day of the disease. Occasionally they may fail to appear in cultures for one or more days during the attack. It is evident that the morbid phenomena must be ascribed to the absorption of toxic substances formed during the growth of the spirillum in the intestine. In cases which terminated fatally after a very brief sickness Koch found but very slight changes in the mucous membrane of the intestine, which was slightly swollen and reddened; but in more protracted cases the follicles and Peyer's patches were reddened about their margins, and an invasion of the mucous membrane by the organisms was observed in properly stained sections. They penetrated especially the follicles of Lieberkühn, and in some cases were seen between the epithelium and the basement membrane. As a rule, the spirillum is not present in vomited material, but there are numerous exceptions to this rule on record. All observers have found the organism always present in cases of true cholera; on the other hand, very numerous control experiments fail to show its presence in the intestinal contents of healthy persons, when cholera is not prevalent, or in that of those dead from other diseases.

Nicati and Rietsch observed a certain degree of attenuation in the pathogenic power of the spirillum, after it had been cultivated for a considerable time at from 20° to 25° C., and the observation has since been made that cultures which have been kept up from Koch's original material have no longer the original pathogenic power. They also gradually change in biological characters upon prolonged cultivation, the colonies on gelatin plates being much less glistening and granular.

The organism most likely to be confounded with the cholera spirillum, and from which it must be differentiated by the methods of cultivation, as well as by the aid of the microscope, is the spirillum of Finkler-Prior, otherwise called the vibrio proteus. It was obtained by Finkler and Prior in 1884, from the fæces of patients with cholera nostras, after allowing the dejecta to stand for some days. Subsequent researches have not sustained the view that this spirillum is the specific cause of cholera nostras. Besides this spirillum many others, more or less resembling the spirillum of cholera, have been isolated. With the exception of the vibrio of Ivanoff (Migula), an organism incidentally isolated from the stools of a patient suffering from typhoid fever, none of these spirilla agglutinate with cholera immune serum. The colonies of this vibrio, however, do not closely resemble those of cholera on gelatin plates, being less granular and more filamentous.

Despite the numerous controversies on the subject since the first announcement by Koch that he considered his spirillum to be the cause of cholera, and the many assertions to the contrary, the relationship between the two is to-day admitted by practically all authorities. The opinion to this effect is based upon a number of reasons, some of which are as follows:

1. The spirillum of Koch has never been found in any other disease, a point that has been established by innumerable observations.

2. This spirillum is found in all cases of Asiatic cholera, without exception, provided that the case is not too far advanced. In such a case there has been a secondary infection, that has killed out the true organism and masked its effects. Ever since the first announcement of this discovery by Koch, observers have verified his assertions in all parts of the world where cholera has been investigated.

3. This spirillum is found in slight cases as well as in severe. It is present in the beginning of the attack, and it is located in the intestine, that is to say in the region especially attacked by the disease, and in which occur the initial and essential lesions.

The attempts to add to these arguments the more decisive one of successful inoculation experiments, were at the first not satisfactory in their results. Nicati and Rietsch were the first to secure successful results, which they obtained by introducing pure cultures of the organism into the duodenum of guinea-pigs, in which animals they had previously tied the ductus choledochus. By these experiments they obtained symptoms extremely analogous to those of true cholera, and Koch also succeeded in the same direction by passing the infectious material (pure cultures) into the stomach by an œsophageal catheter. In his experiments the animals had been previously narcotized by the injection of tincture of opium, to prevent peristalsis, and their stomachs had been made alkaline by the introduction of carbonate of soda, a solution to make the contents of the stomach

alkaline being necessary, because the spirillum of Asiatic cholera will not develop in an acid medium.

Doyen has shown that by introducing alcohol into the stomach the alkaline solution and the tincture of opium may be dispensed with. But, however the experiments may be conducted, they all show one important thing—the great necessity for a healthy condition of the gastro-intestinal tract for the avoidance of infection with cholera. Dyspeptics and alcoholics have been shown in all epidemics to be especially fatally attacked by the disease. It cannot yet be affirmed that the absolute proof of the production of cholera by the specific spirillum has been obtained, because the methods employed in the experiments mentioned above leave too many loop holes open for the occurrence of accidents, and yet the evidence is so nearly complete that there seems to be no reason for any doubt; the more especially as the exact experimental evidence can probably never be obtained, because none of the lower animals, so far as is known, are susceptible to cholera under natural conditions. The nearest approach to an actual experiment upon man is the case of one of the members of one of the cholera courses held in Berlin in the winter of 1884–85. This man, a physician, was attacked with "cholerine," and after some suffering, but no dangerous symptoms, recovered, the cholera spirillum being isolated from the discharges at various times during his illness. There seems to be no doubt that this was a case of true cholera, arising from some carelessness upon the victim's part in handling the cultures with which he had to deal in the laboratory, for there were no cases of cholera in Berlin at the time, nor had there been for a long time previous.

The famous experiments of Pettenkofer and his pupils and similar experiments by Metschnikoff, in which cultures of cholera spirilla were deliberately swallowed, do not militate against the etiological importance of that spirillum. These experimenters suffered from symptoms similar to those observed in the milder forms of epidemic cholera, and the dejecta were similar in character and contained the spirilla in like numbers.

The entrance of the spirilla is undoubtedly effected by means of the gastro-intestinal tract, and there has not been a particle of evidence from experimental work to favor the theory of Pettenkofer that it may enter from the air and through the respiratory organs.

The acidity of the gastric juice is extremely unfavorable to the growth of the organism, and this explains the liability of the persons with functional or organic disease of the stomach to attacks of the disease, for in these instances the reaction of the gastric juice is altered or modified so as to allow the spirillum to pass this point of danger and reach the intestine, where there are more favorable conditions for its development. Diluted hydrochloric acid (0.05 per cent.) is said to kill the spirillum in six minutes. In the presence of pepsin 0.019 per cent. of acid suffices. Water, taken on an empty stomach, excites very little acid secretion—in fifteen minutes from 0.011 to 0.03 per cent. These quantities are entirely too small to prevent the passage of the organism.

Nicati and Rietsch, and Van Ermengen determined the toxicity of cultures of this organism when they had been deprived of the bacteria by filtration or when the bacteria had been killed by heating. In 1885 Nicati and Rietsch, by treating similar cultures with alcohol, succeeded in extracting a substance that killed guinea-pigs and rabbits, with the production of cramps and a lowering of temperature. Brieger studied the various chemical bodies that appeared in the cultures of the cholera spirillum; among the number there were convulsivants, methyl guanidin and a base, $C_3H_8N_2$, a febricant poison, and compounds that produced inflammation and necrosis. More recently, Brieger and Fraenkel have isolated a toxalbumin, and Petri has determined the presence of a less active substance, toxopeptine.

Hueppe and Scholl have perhaps made as important researches as any in their work upon cultures that have been deprived of free access of oxygen. From such cultures they succeeded in obtaining a peptoxin that in a dose of 5 c.c., killed guinea-pigs in forty minutes, the animal presenting paralytic symptoms after ten minutes and convulsions after a quarter of an hour. This is a more active poison than was obtained before and was got in larger quantities; an egg after inoculation with a pure culture produced at the end of eighteen days enough to cause the death of ten guinea-pigs. The importance of this is seen when it is remembered that the spirilla are deprived of the access of oxygen when they are developing in the human intestine, and according to these experiments are therefore under the most favorable conditions for the development of this particular toxin.

Numerous experiments have shown that fluid artificial media do not usually become very toxic when cholera spirilla are grown in them. If they be filtered before the vibrios have died off to any considerable extent the filtrate is not highly toxic, while the residue, consisting largely of the bacteria themselves, is toxic in very much greater degree, even if heated sufficiently to kill the bacteria. That diffusible toxins may be produced in the animal body was shown by Metschnikoff, Roux, and Taurelli, who sealed cultures of cholera in collodium capsules which were introduced into the peritoneal cavities of animals with fatal results. The chemical nature of these various toxic substances is unknown.

A temperature of from 30° to 40° C. is the most favorable for the development of the cholera spirillum, but it will grow slowly at a temperature as low as 17° C. It ceases to grow at a temperature lower than this, but its vitality is not destroyed, and it grows well when the temperature is again raised; at −10° C. its vitality has been retained, but, on the other hand, heating to a temperature as low as 56° or 60° C. is sufficient to destroy its vitality in a short time.

Inasmuch as no true spore formation has been seen to occur in the development of this organism, it is not surprising that drying was shown, first by Koch, to destroy its vitality in a very short time—less than twenty-four hours. But conclusions drawn from his experiments may be misleading, for while this destruction of vitality by drying does occur in a very short time in the case of thin layers, it does not take place under less favorable conditions. This was shown by Kitasato, and by Berkholtz, who saw the vitality retained, the one for thirteen days and the other for thirty-eight, in experiments in which silk threads were used for holding the organism during their subjection to desiccation. It should be said, however, that these experiments were conducted in a desiccator, which did not permit the free access of oxygen to the bacteria, and it is undoubtedly the case that this agent is as important as any in the production of the result that it was desired to obtain. On the other hand, desiccation was probably more complete than would usually be the case under more natural conditions.

The organism has been found in ordinary drinking-water by Koch in one of the tanks in India, in the neighborhood of which an epidemic of cholera had broken out. It does not live long in distilled water, however, as shown by Meade Bolton, Wolfhügel and Riedel, and others. Strauss and Dubarry found that it lived for fourteen days in one case, and Kraus, for two days only. Other observers have not seen it retain its vitality for anything like so long a time. In ordinary sterilized water it lives longer, according to the experiments of Wolfhügel and Riedel, as well as Pfeiffer, who found that it existed for seven, nine, and twelve months, while Hochstetter lengthened this time to three hundred and ninety-two days. And more recently viability has been observed after nearly two and a half years. Its vitality appears to be shorter again in non-sterilized water. Strauss and Dubarry found it to be thirty days in one specimen, and thirty-nine in another; while a mixture of other bacteria shortens the time still more. This latter point is one of great importance and has been studied by many experimenters. Koch determined that the organisms ceased to live in ordinary drinking-water at the end of six or seven days, and that after twenty-four hours' contact with sewer water they appeared to be dead;

while Schiller, on the other hand, found that they retained their vitality in the same medium for fourteen days. Petri, in an effort to find out how long they lived in the intestine after burial, was able to demonstrate them in cultures at the end of nineteen days. Certain foods may be of great importance in transmitting the organism, as in the case of milk, in which it grows with great energy and without producing the least visible alteration; it has been shown that it will live for at least four days in milk and forty-eight in butter.

Most of these experiments were conducted with the idea that this organism is an aërobic one, but Hueppe has shown that it is also anaërobic, and that grown under these conditions the spirillum is possessed of a greater virulence, but it is also easier of destruction. As suggested by Proust, this may explain the comparative rarity of *immediate* infection. The bacterium coming from the intestine as an anaërobic organism is possessed of feeble resisting powers and is therefore easily destroyed, and it is only after it has taken on the conditions of aërobic growth that are furnished it in the medium in which it develops outside of the body that it finds itself possessed of the power of resistance sufficient to enable it again to enter the human body. Such observations are of especial interest in connection with the theory of Pettenkofer (*vide supra*), as seeming to show that his idea of the influence of locality is exact, in so far as this influence is exerted in changing the anaërobic to aërobic conditions of growth and effecting an adaptation of the organism to this change.

According to Koch, solutions of 1 in 400 of carbolic acid, 1 in 2,500 of sulphate of copper, and 1 in 10,000 of corrosive sublimate are sufficient for the arrest of the development of the spirillum of Asiatic cholera. Esmarch and Eisenberg show that creolin will destroy it more quickly than carbolic acid in solutions of the strength of from 1 in 1,000, or 1 in 2,000. Liborius, Kitasato, and Pfuhl have shown the active effect of freshly prepared milk of lime, while Hueppe and Loewenthal convinced themselves of the important prophylactic and therapeutic value of salol in the management of cholera.

Treatment.—*Inoculation Against Cholera.*—The first efforts to confer active or passive immunity to cholera in the human subject were made by Ferran, a Spanish physician (Report to the Academy in Barcelona, July 16th, 1884), who attempted to immunize more than twenty-five thousand people during 1885, when cholera was epidemic in Spain. His method consisted in the subcutaneous injection of increasing amounts of virulent cultures of the cholera vibrio, five or six days being allowed to elapse between successive injections. Three such injections were regarded by him as fully protective against the disease. He also employed injections of blood from those who had recovered from cholera to protect others from attacks of the malady. His enthusiastic claims for the efficiency of these prophylactic measures were discredited by other observers, and there appears to be no doubt that his methods were faulty. The purity of his cultures is open to question and his claims were exaggerated. But his conceptions were the same as those which subsequently led to more careful and promising work in this direction, and the credit of priority belongs to him.

Since these early attempts of Ferran, which were based upon studies of the immunization of guinea-pigs at a time when proper methods had not been elaborated, numerous investigators have experimented on animals in this direction and have obtained results which throw considerable light on the character of the immunity that can be conferred upon animals, and presumably upon man.

One of the difficulties encountered in this work is due to the fact that the lower animals do not respond to cholera infections so as to present a well-defined disease comparable to human cholera. Fatal results may follow intravenous, subcutaneous, or intraperitoneal inoculations with cholera cultures, and also after the introduction of cultures into the stomach. But special preparation of the animals for this last mode of inoculation is usually necessary. The procedure for this purpose, devised by Koch for guinea-pigs, was the neutralization of the stomach contents with sodium carbonate, and the checking of intestinal peristalsis with a subcutaneous injection of tincture of opium. If, after this preparation, the animals receive cultures of the cholera vibrio, introduced through a stomach tube, they develop symptoms which bear some resemblance to the algid stage of cholera. The temperature falls, the skin becomes cyanotic, and great muscular weakness is manifested by inability to walk or stand. Occasional muscular spasms are frequently observed and the animals die after several hours. These symptoms do not develop immediately after the inoculation, and there is evidently a very considerable multiplication of the vibrios in the intestine. At autopsy the serous coat of the intestine is injected, the intestinal wall is swollen, and a serous fluid containing desquamated epithelium fills the bowel. There are usually no evacuations, though occasionally a thin serous fluid escapes from the anus.

While these manifestations bear some resemblance to the algid stage of human cholera, the results of such inoculations cannot be regarded as satisfactory reproductions of this disease. In 1893 Metschnikoff published observations showing that young, suckling rabbits might be inoculated with minute quantities of cholera vibrios placed in the mouth, and that they then developed a fatal disease more closely resembling human cholera than that obtained in guinea-pigs by Koch. This was subsequently shown to be the case when very young kittens or puppies were employed. We shall have occasion to refer to these experiments again.

Experiments with a view of determining the possibilities of immunizing against cholera have been very numerous. Most of the observations have been made on guinea-pigs, though other animals have also been employed. It has not been difficult to attain positive results in many different ways. Intraperitoneal, subcutaneous, or even intravenous inoculations with non-lethal amounts of living cultures of cholera vibrios is followed within a few days by a species of immunity manifested by bactericidal or bacteriolytic properties of the serum of the animal. Such animals will then survive inoculations with virulent cultures in amounts which considerably exceed those regularly fatal to normal animals. Similar results may be obtained by the use of dead cultures, whether the vibrios have been killed by heat or by the addition of germicides. Such animals also are immune against inoculation with virulent cultures in considerable amount. This immunity, whether caused by living or by dead cultures, protects the animals against inoculations into the blood, peritoneum, or beneath the skin; but appears to have little if any effect upon the course of the disease when cultures are introduced into the mouth or stomach. This fact was strikingly manifest in experiments in very young animals, which, as stated above, readily acquire a form of cholera when very small amounts of cultures are introduced into the mouth. Moreover, very large amounts of cholera cultures introduced into the blood or peritoneal cavity cause death in immunized animals in spite of their protection against moderate lethal doses. Large doses of dead cultures also cause death. A fact worthy of note is that filtered recent cultures of the cholera vibrio are neither very toxic nor useful for immunization.

The results of the experiments mentioned above lead to the inference that the introduction into the body of non-lethal quantities of the vibrio calls forth the production of anti-bodies that are destructive to the vibrio if they are brought into contact with it, but that they are not capable of neutralizing toxic substances that appear to be closely associated with the bodies of these micro-organisms if not actually a part of their structure. The immunity obtained is due to bacteriolysis and not to antitoxins. We may, therefore, fatally poison an immune animal with cholera cultures though it be capable of destroying a limited number of cholera vibrios which are brought into its tissue fluids.

It has been shown that the blood and serum from patients who have recovered from attacks of cholera also contain these or similar bacteriolytic substances, but there appears to be no antitoxic substance in these fluids.

These bacteriolytic anti-bodies do not exist to an appreciable extent in the blood of convalescents immediately upon recovery, but are distinctly active about three weeks after the attack, then gradually accumulate or increase in potency until a maximal efficiency is reached between the fourth and sixth weeks. At this time 0.01 c.c. of the blood may be enough to protect a guinea-pig from the effects of an otherwise fatal intraperitoneal infection with cholera. After the sixth week the bacteriolytic value of the blood gradually declines and is lost after about three months.

To emphasize still further the character of this immunity, experiments may be cited which show that animals which have been inoculated with cholera vibrios in amounts ordinarily sufficient to kill, may be saved if they receive injections of serum from immunized animals within from one-half to two hours after the inoculation, before symptoms referable to intoxication have developed. When these symptoms have declared themselves the treatment is without avail, *i.e.*, if the disease can be checked by destroying the vibrios already in the system, the immune serum will protect; but if there is already in the body a dose of toxic substances sufficient to kill, the immune serum is powerless to neutralize them. These toxic substances appear to be present in lethal quantities in the majority of cases, as soon as symptoms of disease become manifest.

A question of great practical importance is whether these protective, bacteriolytic anti-bodies which are present in the blood and lymph can pass into the digestive tract and act upon cholera vibrios present in the intestinal contents. Experiments upon animals, already cited, appear to answer this question in the negative, but it is doubtful whether these results can be directly applied to man. If Ferran's claims are justified by the facts, such direct application of animal experiments cannot be made; for an active immunity caused by subcutaneous injections of cholera vibrios would appear to protect against infection by way of the mouth in human subjects, though they failed to do so in animals. It was the belief that such was the case that induced Haffkine to undertake the immunization against cholera by a method essentially similar in principle to that employed by Ferran, but safeguarded by a more highly developed technique.

Haffkine experimented with his method of immunization in India, aided by the Government, and between 1893 and 1895 had subjected about forty thousand people to his prophylactic treatment. This consisted in the subcutaneous injection of living cultures of the cholera spirillum of definite and known virulence. The first injection was made with a culture of moderate virulence, attenuated by long artificial cultivation and taken by him to India from the European laboratories.

These injections were made only after a microscopical examination of a stained smear had failed to reveal contamination of the culture and revealed well-formed, apparently normal cholera vibrios. The injections were made under strictly aseptic conditions. During the first two hours after the injection there were no appreciable effects either locally or constitutionally. Between the third and twelfth hours there was a gradually developing tenderness at the point of inoculation with general malaise and fever. In normal cases the fever reached 101° F., but would sometimes reach 104° when the susceptibility of the patient was great. The amount of culture injected depended upon the age of the patient; for an adult man the amount being about 1 c.c. From the twelfth to the thirty-sixth hour after the inoculation the general symptoms gradually but completely vanished and a painful induration at the point of inoculation developed. This also subsided in the course of a few days. No digestive disturbance was occasioned by the inoculation, and no change of diet or occupation was necessary.

The second inoculation was made about five days after the first. For this purpose a highly virulent culture, kept active by passage through susceptible animals, was employed, the dosage being determined by the reaction obtained after the first injection. The effects of this inoculation were essentially the same as those obtained after the first, but were usually less pronounced. The immunizing action was believed to be complete six days after the first inoculation. Up to 1896 over one hundred thousand people are said to have received this treatment.

The results of this treatment, which was purely preventive, not curative, are reported as being very promising. Several of those so treated contracted cholera shortly after the first injection, showing that its protective action was not immediate. Haffkine believed that the full protective action was attained in about twenty days. Comparative statistics, when of a given group about half were inoculated, were greatly in favor of the value of the method. The protection was not lasting, however, and seems to have gradually passed away, some twelve months being the probable limit of its efficiency. The protection is not absolute, and the mortality among those who have been inoculated and yet acquired the disease is but slightly less than among the uninoculated. About one-nineteenth as many cases occurred among the inoculated and about one-seventeenth as many deaths. Of late years this method appears to have fallen into disuse. This is not surprising when the difficulty of inoculating a whole population, the evanescent character of the protection, and the uncertainty of its absolute value are considered.

Upon theoretical grounds, as already stated, but little can be expected from a bacteriolytic serum injected beneath the skin in human cholera; for the vibrios are situated in the intestinal contents and the crypts of the intestinal mucosa.* To be effective the protective constituents of the serum must come in contact with the bacteria they are to destroy. It appears doubtful whether these elements enter the intestinal lumen when present in the blood. A serum which had antitoxic properties should be much more efficient. Pfeiffer has shown that the most active toxic substances produced by the cholera vibrio are intimately connected with the bodies of the organisms when the latter are grown in artificial media. In 1896 Metschnikoff, Roux, and Taurelli-Salimbeni made experiments with a view of demonstrating that soluble toxins might be obtained from the cholera vibrio as a species of secretion. They obtained a highly poisonous toxin, not destroyed by boiling, of which one-fourth of a cubic centimetre killed a guinea-pig weighing 300 gm. in eighteen hours. They also showed that it was possible to obtain an antitoxic serum by immunizing animals with this toxin. But this serum failed to cure young animals infected by the mouth with cholera vibrios. As yet, therefore, there is no known serum therapy for cholera.

In the absence of a specific antitoxic or other remedy for cholera, recourse must be had to measures directed against morbid conditions as they arise.

A very great number of remedies have been employed with a view of destroying the cholera spirilla in the intestinal tract, or, at least, of inhibiting their multiplication. Among these remedies are: chlorine water, mercuric salts, salts of copper, iodine, iodoform, creosote, creolin, cresol, resorcin, thymol, pyoktanin, benzoic acid, salicylic acid and its salts, salol, tribromsalol, tribromphenol, bismuth, benzoyl-acetyl peroxide, etc. It cannot be said that the clinical evidence in favor of any of these remedies is strong, and upon theoretical grounds their utility is very doubtful since the great dilution they suffer in the intestinal tract must render them almost inert. The same appears true of the proposed treatment with mineral acids in eight- to ten-drop doses, diluted with water.

We have already seen that during epidemics of cholera mild cases of this disease are of not infrequent occurrence. These cases are indistinguishable in many in-

* The efficacy of the bacteriolytic serum when administered by mouth or in enemata does not appear to have been tested. It would be worthy of trial.

stances from attacks of simple diarrhœa due to intestinal irritation or indigestion, though frequently unaccompanied by pain. The only safe rule at such times is to regard all cases of diarrhœa as choleraic and as the possible beginning of a serious attack. The patient must be put to bed and isolated. The dejecta should be regarded as likely to contain the cholera spirilla, and carefully disinfected before being disposed of. A warm bath, with warm compresses on the abdomen, has been recommended. The diet should be restricted to fluids, previously boiled. Thirst may be relieved with boiled or carbonated (not alkaline) water. There are differences of opinion regarding the measures appropriate to the treatment of the diarrhœa. The usual practice is to employ some preparation of opium to check the discharges. The tincture given in small, frequently repeated doses has given good results. As it is important to allay all intestinal irritation it must be a matter of judgment in each individual case whether it be wiser to endeavor at once to check the diarrhœa or whether a freer evacuation of the bowels to discharge any irritating contents should be attempted. For the latter purpose calomel in repeated moderate doses, given until the stools become greenish, has a good reputation. Castor oil, emulsified with mucilage of acacia, peppermint water, and syrup, has also been employed. It is thought that calomel is partially converted into mercuric chloride in the intestine, and that it thus exerts some antiseptic action; but to what extent this is true is not known. As an antiseptic sodium sulphocarbolate, in fifteen- to twenty-grain doses for children and thirty-grain doses for adults, repeated every three or four hours, has been used with asserted beneficial effects. To check the diarrhœa, besides opium, astringents have been used and recommended, and to relieve pain the compound tincture of camphor has been employed. The prevalent opinion, however, is that opium fulfils the requirements better than other drugs, and that rest, warmth, and an appropriate diet are of the utmost importance. Tea and moderate stimulation with brandy may be used according to the indications.

Should the symptoms persist and vomiting set in notwithstanding the treatment indicated above, the copious enemata of tannic acid, recommended by Cantani, may be resorted to.

Long before the epidemic of 1866 Dr. Murray, in India, had recommended the half-hourly injection of a pint of a weak solution of common salt and carbonate of sodium into the rectum at a temperature of 120° F., and is said to have obtained very striking results. Similar means were employed by Sansom (*The Practitioner*, November, 1892), in 1866. Cantani advises the addition of tannin to the hot water. From eighty to three hundred and twenty grains are dissolved in three pints or a quart of water or chamomile infusion at a temperature of 102° to 105° F., and twenty drops of laudanum and an ounce or an ounce and a half of gum acacia are added. Instead of tannin, thymol in solution of hot water (1 in 1,000) has been recommended by other authorities. In the recommendations of the Royal College of Physicians (1892), benzoate of sodium, two drachms to a quart of water, has been suggested as an alternative to the tannic acid. In every case the injection should be made with much gentleness. The best position of the patient is that on the back with the hips well raised and the legs well drawn up as for lithotomy. The reservoir douche enema should be used and not the ordinary pump. There is much room for doubt as to whether the addition of any medicament to the hot water is of any special value, the favorable results being due probably to the clearing away of irritant and offensive *débris*, to the absorption of fluid from the intestinal surface, and to the relaxation of the arterial spasm by the hot and moist application; but up to the present time the use of tannic acid persists and is recommended. If more than two quarts are injected, a weaker solution should be employed. These enemata may be repeated several times in twenty-four hours. As shown by Cantani, the hot saline solution may pass through the ileo-cæcal valve into the small intestine.

If signs of improvement do not soon follow the procedure described above, and the algid stage of the disease supervenes, recourse should be had to the second method, of introducing fluid recommended by Cantani and called by him "hypodermoclysis," and consisting in the injection of a hot saline solution into the subcutaneous tissue. About one drachm of common salt is dissolved in a quart of distilled water at a temperature of 100° to 105° F. The apparatus for this should consist of a glass funnel with a long rubber tube attached to a hypodermic needle of fairly large calibre. The needle is introduced in the gluteal, interscapular, lumbar, or iliocostal region, the funnel being held at about the level of the patient, and the needle pushed so far in that it may be moved freely in the subcutaneous tissue. The reservoir is then elevated slowly so that the fluid runs into the tissue by the force of gravity and its distribution is aided by the manipulation of the fingers. When about half of the fluid has been introduced the needle is removed and the remainder is injected in another place. The method seems to be rational and is supported by strong evidence by Cantani, who has made extensive use of it. It was also extensively employed in the Hamburg epidemic. It is easier of application than the older method of intravenous injection that has been employed for many years, and it seems to be attended with better permanent results. Either or both of these methods must be employed earlier than is usually the case, and before the actual symptoms of death have made their appearance; to wait too long is to throw away all chances of success. The amelioration of the symptoms is usually very striking and prompt, due to the introduction of fluid and warmth; but improvement is frequently of short duration. The procedure may be repeated if the indications for it return; but experience has led to the belief that three or four injections of a quart or more are all that are likely to be beneficial.

Rest and quiet being of the greatest importance, owing to the exhausting nature of the disease, it must be a matter of judgment to what extent active measures to combat the conditions as they arise are wise. The patient should be kept as quiet as is compatible with proper care.

During collapse the condition of the circulation excites most solicitude. When the pulse at the wrist is lost and cyanosis appears, the most efficient remedy is the injection of fluid either intravenously or beneath the skin, as already described. Where the loss of fluid is less pronounced, careful stimulation with cold champagne or brandy and water may be tolerated by the stomach. Subcutaneous injections of ether or nitroglycerin, if used with care and not contraindicated by the condition of the patient, may give good results. Inhalations of small doses of amyl nitrite may also prove beneficial. In the early stages of the disease opium may be used to relieve pain, for it also tends to check the diarrhœa. But in the later stages, when there is danger of collapse, this drug should be avoided. Pain must then be relieved by other means, such as hot applications, moderate counter-irritation, inhalations of chloroform, or subcutaneous injections of camphor rubbed up with olive oil in the proportion of one part of camphor to nine parts of oil sterilized by heat. Gentle massage may give relief from pain, but is likely to disturb the patient more than is wise.

Thirst can best be relieved by ice held in the mouth, cold carbonated water, or nourishing fluids given in small amounts and at frequent intervals.

To prevent loss of heat, the patient should be kept in a warm room, the skin should be kept as dry as possible without disturbing the patient, and he should have dry heat applied by means of hot-water bottles or warm bricks; or the temperature may be maintained by hot compresses.

After recovery from the severe stage of the disease the treatment must follow the indications as they arise. Particular attention must be given to the diet, relapses being frequently traceable to neglect in this direction.

Prophylaxis.—Two principles govern the measures

which should be taken to avoid cholera. The first looks to the exclusion of living cholera spirilla from the gastro-intestinal tract; the second refers to preserving any natural resistance, particularly on the part of the intestine, to injury due to the presence of that organism in the intestinal contents. It is believed that the toxins produced by the cholera spirillum are not absorbed through intact intestinal epithelium, but gain entrace to the circulation only after the epithelium has become damaged, necrosed, or desquamated. Therefore all dietary indiscretions which might cause intestinal irritation are to be avoided. Over-fatigue and exposure to cold are to be carefully guarded against. But it appears wise not suddenly to change the ordinary mode of life, but simply to follow the usual habits in a temperate manner. The free use of alcohol appears to be extremely dangerous. Those addicted to its use are particularly susceptible, and when attacked by the disease the prognosis is bad in people of intemperate habits. Care in the character of the food is important. All articles which might carry infection should be avoided entirely, or partaken of only after being cooked. This is especially the case with water and milk, which should be heated to the boiling point. Prolonged boiling is not necessary, but to insure the death of the spirillum it is safest actually to boil liquid articles of food. It has been recommended to take acid drinks, such as very weak hydrochloric acid, as a prophylactic measure, but it seems doubtful whether this is a wise measure, in view of the danger to the digestion if sufficient acid be taken to act as an effective agent in killing the spirillum. Particular care should be exercised against infection by those attending cases of cholera. They should disinfect the hands immediately after they have come in contact with the dejecta or vomitus from the patient. A two- or three-per-cent. solution of carbolic acid, 1 in 1,000 solution of mercuric chloride, or a solution of "chloride of lime" may be used for this purpose. It is possible that peroxide of hydrogen might find useful application for this purpose and in cleansing the patient, particularly for rinsing the mouth; its freedom from toxic properties and odor and its acid reaction particularly commending it.

The public measures for preventing the spread of cholera must be directed toward the destruction of the spirillum, and, when that is not possible, the checking of its dissemination. Each case that occurs must be regarded as a possible centre from which other cases may arise. The patient must, therefore, be isolated and the utmost care taken to destroy all the spirilla in the dejecta and vomitus, on the bedding and clothing, and on the hands or persons of those attending him. As the patient must be kept as quiet as possible, the evacuations must be received in a bed-pan and disinfected before being disposed of. For this purpose milk of lime has been found very efficacious. This may be prepared as follows: One volume of quicklime, which must not be air-slaked, is placed in a large vessel containing an equal volume of water. This is gradually absorbed by the lime, which then falls to powder. Three volumes of water are then added and the whole is stirred to a thin creamy fluid. Of this equal parts should be added to the dejecta and the mixture allowed to stand for an hour, when disinfection may be considered complete. Fresh "chloride of lime" may also be used, a large heaping tablespoonful of the powder being added to each quart of the evacuations and thoroughly mixed with them. In half an hour the mixture may be regarded as harmless. The hands of the attendants should be disinfected immediately after coming in contact with the patient. The supernatant fluid obtained by mixing 2 parts of fresh "chloride of lime" and 100 parts of water, shaking, and allowing the sediment to settle, may be used, or a two- to three-per-cent. solution of carbolic acid, or 1 in 2,000 corrosive sublimate. These solutions may also be used to cleanse the patient. Sheets and linen may be soaked in 1 in 1,000 solution of corrosive sublimate, the above solution of carbolic acid, or in a three-per-cent. solution of green or soft (potash) soap, with or without the addition of five per cent. of crude carbolic acid. The fluid must completely cover the articles. The simple soap solution must act for twenty-four hours; the carbolized soap solution will disinfect within twelve hours. Weak formalin, two per cent., may also be used where its odor and irritating properties are unobjectionable. In emergencies, where facilities for carrying on such disinfection cannot be obtained, boiling or burning may be employed to destroy the spirilla.

The bodies of the dead should be disinfected or wrapped in a sheet wet with 1 in 1,000 corrosive sublimate solution, and placed in a tight coffin upon a layer of some absorbent material. The sick-room must be disinfected with sulphurous acid or formaldehyde, or thoroughly washed with 1 in 1,000 corrosive sublimate, and be well aired and dried out before being again occupied.

Harold C. Ernst.

Revised by *Edward K. Dunham.*

BACTERIOLOGICAL TECHNIQUE.—The methods for the artificial cultivation of bacteria are of fundamental importance in bacteriology, and for that reason deserve very careful consideration. Nutrient media of various kinds are used, but the three most commonly employed are bouillon, gelatin, and agar. These in turn may be variously modified as the needs of the work may require. In addition, other media are used, such as blood, serum, exudates, eggs, urine, milk, potatoes, and the like. These will be severally considered.

Bouillon.—To prepare beef tea, or bouillon as it is called, 500 gm. of lean, chopped beef (Hamburger steak) are placed in a suitable enamelled vessel or in a one-and-a-half-litre flask and 1,000 c.c. of ordinary tap water are added, and the whole is thoroughly mixed. This may now be set aside in an ice-box for twenty-four hours so as to bring the soluble constituents into solution; or, what is preferable, it may be placed in a water-bath and warmed at a temperature not exceeding 60° C. for an hour. In this way the nutrient substances are dissolved out and much time is saved. It is not desirable at this point to heat the fluid above the temperature given, inasmuch as that would lead to the coagulation of the albuminous constituents, which, if they are allowed to remain in solution, will facilitate the subsequent clarification of the medium. When the digestion is completed, whether carried out at a low temperature or in the water-bath, the liquid is strained through well-washed, starch-free muslin, or the juice may be expressed by means of a meat press. The liquid thus obtained is of a dark red appearance, due to the presence of hæmoglobin.

One thousand cubic centimetres of the meat extract are then placed in a clean flask or vessel, and 10 gm. of dry, powdered peptone (Witte's) and 5 gm. of common salt are added and the whole is then warmed at about 55° to 60° C. till the peptone has dissolved. The next step is to render the medium suitably alkaline, since bacteria as a rule require a slightly alkaline soil. This manipulation requires special care, for, if improperly done, the finished product may be cloudy, or may even have a deposit, or may even be unfit for the growth of bacteria. The clouding and the formation of a precipitate can be avoided by boiling the meat extract after adding just enough alkali to neutralize the fluid. For this purpose 5 c.c. of *normal* sodium hydrate (four-per-cent. solution) are added to the litre of meat extract. This amount is usually sufficient to make the extract neutral to litmus. The liquid is then heated in a boiling water-bath or over a free flame for about fifteen minutes, after which it is filtered through a moist plaited filter and allowed to cool to about 50° C. As stated, bacteria thrive best when the medium is slightly alkaline. Hence 10 c.c. of the normal sodium hydrate are now added to impart the desired alkalinity, after which the liquid is again boiled for twenty to thirty minutes, and finally filtered through moist paper.

Inasmuch as considerable water is usually lost by vaporization during the preparation of the medium, it is advisable either to indicate the volume at the beginning

of the operation by a suitable mark on the vessel or better, to take the weight of the fluid before and after heating. The difference in the volume or weight is finally made up by the addition of the corresponding amount of distilled water. The finished bouillon should make up to the original volume of meat extract, that is, 1,000 c.c.

The beef tea thus prepared is now filled into tubes or into flasks, as the case may be, and sterilized by steam. This process will be described later. It is hardly necessary to add that the bouillon after being tubed and sterilized should be perfectly clear, without a deposit, and should have a slight alkaline reaction.

For cultivating the gonococcus Thalmann recommends using the ordinary bouillon, to which has been added two-thirds to three-fourths of the amount of alkali necessary to make it neutral to phenolphthalein.

Sugar-free Bouillon.—The bouillon as just prepared always contains some sugar derived from the muscle tissue employed. For many purposes this sugar content is undesirable, and must be removed in some way. One procedure is to allow the meat extract to ferment at a low temperature, 10° to 15° C., for two days. Another is to place the meat extract at 37° C. for twenty-four hours. Neither one of these methods will give results which can be relied upon. The best procedure is to add to the meat extract a rich fluid culture of some acid-producing organism, such as Bacillus coli (Smith), or B. lactis aërogenes (Durham), and then set it aside to ferment at 37° C. for twenty-four hours or longer. The frothy liquid is then carefully neutralized by the addition of normal sodium hydrate, peptone and salt added, then boiled, cooled, and rendered alkaline according to the directions given under the preparation of bouillon. The sugar-free bouillon thus prepared does not contain indol, as might at first be supposed. It is preferable to the Dunham peptone solution mentioned below for testing for the presence of indol, since a good reaction is given in sixteen hours, whereas the cultures in Dunham's solution often require several days before giving a positive test.

Martin's Bouillon.—The thoroughly mixed meat suspension (500 gm. of chopped beef and 1,000 c.c. of water) is set aside at about 37° C. for twenty hours so as to destroy the sugar normally present. The liquid is then strained through well-washed muslin, and to 1,000 c.c. of the filtrate 5 gm. of common salt are added, after which the liquid is neutralized and finally rendered alkaline by the addition of 7 c.c. of normal alkali per litre of bouillon. Ordinary peptone is not added, inasmuch as it is likely to contain sugar. Instead, Martin adds to this bouillon an equal volume of a rich peptone solution made by digesting the stomach of a pig. This latter solution is prepared as follows: A pig's stomach is cleaned and cut up into small pieces, and to 200 gm. of this finely divided tissue 1,000 c.c. of water and 10 c.c. of concentrated hydrochloric acid are added and the mixture is set aside at 50° C. for about twelve hours. The digested fluid is then decanted through a filter of absorbent cotton and the strongly acid reaction is reduced by the addition of 25 c.c. of a sixteen-per-cent. solution of sodium hydrate. The liquid is then carefully neutralized, after which it is rendered alkaline by the addition of 7 c.c. of normal sodium hydrate per litre. The mixture of equal volumes of the sugar-free bouillon and the peptone solution is heated, filtered, and tubed or placed in flasks.

Peckham's Bouillon.—This is made by taking finely chopped beef, which must be as old as it can be obtained in order that it may be free from muscle sugar, and adding 225 gm. of it to 500 c.c. of water. The mixture is rendered slightly alkaline with sodium carbonate, after which it is placed in a water-bath at 40° C., and 4 gm. of trypsin are added. After digesting for an hour the fluid is again rendered alkaline with sodium carbonate. In from one to one and a half hours the digestion should be arrested, otherwise traces of indol may be detected. At the end of this period the mixture is boiled and strained through gauze and filtered cold through wet filter paper to remove the fat. Five grams of salt and enough water to make up to one litre are then added. The acidity of the clear straw-colored filtrate is then reduced to the desired point. The most suitable reaction for the development of colon and like bacilli is when the medium contains such an amount of free acid as to require from 20 to 30 c.c. per litre of a decinormal sodium-hydrate solution to bring it to a point neutral to phenolphthalein.

Artificial digestion of muscle tissue by means of pepsin and trypsin is resorted to in the preparation of Deycke's agar.

Dunham's Peptone Solution.—This is prepared by dissolving 10 gm. of Witte's peptone and 5 gm. of common salt in 1,000 c.c. of ordinary tap water. The solution is then tubed and sterilized by steam. This medium is used to detect the formation of indol by bacteria, but inasmuch as many organisms fail to grow in it and others require several days before giving a reaction, it has not been found to be as suitable as the sugar-free bouillon given above.

Glucose Bouillon.—This is used to test for acid and gas production. It is made by adding to the ordinary bouillon, or better to that which is sugar-free, one or two per cent. of glucose. The two-per-cent. solution is most commonly employed. The sterilization of sugar-containing media by steam requires special care to prevent oxidation of the carbohydrate present. As a rule the steaming should not exceed ten or fifteen minutes each day on three successive days.

Instead of glucose other carbohydrates may be added to the bouillon in one- or two-per-cent. concentration. Thus galactose, lactose, saccharose, maltose, dextrin, and the alcohol mannite are frequently used to differentiate between organisms which otherwise closely resemble each other.

Glycerin Bouillon.—This is especially used for cultivating the tubercle bacillus. It is made by adding five per cent. of glycerin to the ordinary bouillon. The mixture is then tubed and sterilized in the usual way.

Carbolic Bouillon.—This is made so as to contain 0.1 per cent. of carbolic acid. One gram of acid may be added to one litre of bouillon. The better procedure is to add 1 c.c. of a one-per-cent. carbolic acid to 9 c.c. of bouillon. It is advisable to incubate the tubes for several days so as to eliminate any possible contamination. The medium is useful for examining water for the colon bacillus, especially when the bacterial contents are very high. The presence of the antiseptic serves to check or prevent the growth of many organisms which would otherwise develop. It should be borne in mind that weak colon and typhoid bacilli are likewise restrained.

The tubes after inoculation with the water are incubated for twenty-four hours at 38° C., after which lactose litmus agar plates are made, which are then examined for red colonies. Of course all red colonies are not to be regarded without further study as the colon bacillus.

Parietti's Bouillon.—A mixture of carbolic acid and hydrochloric acid is first prepared by adding 4 c.c. of the latter to 100 c.c. of a five-per-cent. carbolic solution. This solution after standing a few days is added in portions of 0.1, 0.2, 0.3 c.c. to portions of 10 c.c. each of sterile bouillon.

Colored Bouillon.—Various coloring agents are added to the nutritive media in order to bring out the acid-producing or the reducing properties of bacteria. The substances which are most commonly used for this purpose are litmus, neutral red, saffranin, and sodium indigo sulphate. The first two are particularly useful, and are prepared the same as the corresponding agar or gelatin media, which see.

Gelatin.—The ordinary nutrient gelatin is really nothing more than bouillon to which ten per cent. of gelatin has been added so as to impart solidity with the additional advantage that the medium is transparent. The method of preparation is as follows: To 1,000 c.c. of the meat extract, prepared according to the directions given under bouillon, 100 gm. of the best sheet gelatin are added; likewise 10 gm. of Witte's peptone and 5 gm. of common salt. The whole is then warmed in a water-

bath at 60° C. until the gelatin has passed into solution. The liquid is then neutralized and enough alkali added in excess so as to impart a suitable alkalinity. As ordinarily prepared the nutrient gelatin requires from 30 to 35 c.c. of normal alkali to effect neutralization. An additional 10 c.c. will give the desired alkalinity. Hence 40 c.c. of the normal alkali may be added at once and the liquid tested with litmus paper. If the liquid is not distinctly alkaline more of the reagent may be added until the desired alkalinity is obtained. The method of standardizing media by means of phenolphthalein will be given later.

When the proper amount of alkali has been added to the gelatin solution the latter is then placed in a water-bath, the water of which is then raised to the boiling temperature. The gelatin is kept immersed in the actively boiling water for three-quarters to one hour. The albuminous constituents of the meat extract coagulate in flakes, and at the same time clarify the liquid so that on subsequent filtration the gelatin will be perfectly clear. The gelatin is then filtered through a plaited filter, which should, however, be first warmed by passing through it several hundred cubic centimetres of boiling water. If the paper and funnel are sufficiently warmed in this way there is no likelihood of the gelatin solidifying on the filter. The filtered gelatin should be perfectly clear, should possess a slight alkaline reaction, and should solidify when cooled under running tap water. If it meets these requirements it is then filled into sterile tubes to a depth of one and a half to two inches, and the entire lot of tubes are then sterilized by steaming for a quarter of an hour on each of three consecutive days.

Whenever nutrient gelatin is mentioned in bacteriological work it is understood to be a ten-per-cent. solution. This medium melts at about 23° C. That is warm summer temperature, and for that reason it is sometimes advisable to add more gelatin to the preparation in order to make it more solid. A twelve- or even a fifteen-per-cent. solution of gelatin is used under these conditions. Again, at other times it is desirable to employ a gelatin which is relatively quite soft, and in that case a five- or eight-per-cent. solution may be made use of. Obviously the amount of alkali necessary to neutralize such media will vary from that required for the ordinary gelatin. The great value of the gelatin medium lies in the fact that it can be readily melted and again resolidified, and in its transparency. Moreover, many bacteria give rise to soluble ferments or enzymes which peptonize or liquefy the gelatin, whereas others are not able to do this. It becomes possible therefore to divide bacteria into two large groups, according as to whether they liquefy or do not liquefy gelatin.

Glucose Gelatin.—This is made by adding to the clear filtered gelatin, prepared as above, two per cent. of glucose. The material is then tubed and sterilized the same as ordinary gelatin. This medium is particularly useful for the cultivation of anaërobic bacteria.

Glucose Litmus Gelatin.—To the glucose gelatin a concentrated solution of litmus is added so as to impart to the medium a deep blue color. This is then tubed and sterilized. During the steaming of this medium the litmus is usually decolored, but on subsequent cooling the blue color returns. If such a medium is overheated in the process of sterilization the sugar will be altered, and as a result the color of the litmus will change to more or less of a red.

For special purposes other sugars may be added to the gelatin, as in the case of bouillon. A lactose litmus gelatin is very useful in differentiating various organisms. The amount added is usually one or two per cent.

Elsner's Medium.—The addition of gelatin to a potato extract, instead of to a meat infusion, was first resorted to by Holz. Elsner's medium is essentially Holz's potato gelatin, to which one per cent. of potassium iodide is added. It can be used to good advantage in differentiating between the typhoid and colon bacilli, but at the same time it should be remembered that it does not afford an absolute means of detecting the former organism. The method of preparation is as follows: 1,000 gm. of well-cleaned potatoes are cut up into lumps which are then mashed as fine as possible, which can be done best by passing the material through a fruit press. The finely mashed potatoes are then placed in a meat press and pressure is applied. In this way about 400 c.c. of a dark liquid is obtained from the kilogram of potatoes. The potato juice is then set aside in an ice chest overnight, after which it is filtered through cotton. Ten per cent. of gelatin and one per cent. of potassium iodide are then added to the dark liquid, and the mixture is warmed at about 40° C. until the gelatin melts. Inasmuch as the reaction of this material varies considerably it is necessary now to determine the exact degree of acidity present, and then to reduce this by the addition of the proper amount of alkali, so that the resulting medium has an acidity such that it would require the addition of 20 c.c. of normal alkali per litre to make the solution neutral. The acidity of the gelatin is determined by titrating a portion, say 10 c.c., with decinormal sodium hydrate, using litmus paper as an indicator. If, for example, 10 c.c. require 3.2 c.c. of the decinormal alkali, it will be necessary to reduce the acidity by adding 1.2 c.c. of decinormal alkali, or better 0.12 c.c. of normal alkali for every 10 c.c. of gelatin made. When the proper degree of acidity has been imparted to the medium, the gelatin is then placed in a boiling water-bath for three-quarters of an hour until all the proteids have coagulated, after which it is filtered through paper, filled into sterile tubes, and sterilized by steaming for fifteen minutes on each of three consecutive days.

Fish Gelatin.—Five hundred grams of chopped fish are added to 1,000 c.c. of water, and the material is digested the same as given above for ordinary gelatin. To the strained liquid 100 gm. of gelatin, 40 gm. of salt, 5 gm. of glycerin, and 5 gm. of asparagin are added, and the mixture when perfectly fluid is rendered slightly alkaline. It is then heated, tubed, and sterilized as above. This medium is particularly useful for the growth of phosphorescing bacteria.

Nutrient Agar.—One drawback to the ordinary gelatin is that it cannot be used as a solid medium at temperatures above 23° C. This has led to the introduction of agar-agar as a stiffening agent. This substance is a seaweed gathered off the coast of Asia. It has no nutritive qualities of its own, and is unacted upon by bacteria. The preparation of nutrient agar is very simple. Ordinary bouillon is first made according to the directions already given. The agar may be obtained as a powder or in threads; in the latter case the agar is cut up into very small pieces, and 20 gm. (two per cent.) is then added to the litre of bouillon, which should be in a large flask, or, better, in an enamelled jar. The vessel and contents should then be weighed, after which the liquid should be gently boiled until the agar has completely dissolved. The vessel is now again weighed, and the difference between the two weights is made up by the addition of the proper amount of distilled water.

It is advisable to place the agar now in a water-bath at about 50° C. for several hours in order to allow the sediment to settle as much as possible. The filtration of a two-per-cent. agar is a very slow and tedious process even when carried out in a steam sterilizer. It is sufficient for practically all purposes to filter through a layer of cotton. The filtrate thus obtained is almost, if not entirely, clear, and whatever little sediment may be present does not in the least interfere with the usefulness of the medium.

The filter is prepared by placing a piece of ordinary cotton, about two inches square, in the angle of a large funnel, and then while it is held down by means of a glass rod, a litre or so of very hot water is passed through, once or twice, so as thoroughly to warm the funnel. Eventually the sedimented agar is carefully and slowly decanted on to the cotton filter. If desirable the agar can be filtered a second time. A very convenient arrangement for the rapid filtration of agar through cotton is shown in Fig. 5052. This consists essentially of

a Witte's perforated porcelain plate, which is steadied in place in the funnel by means of a glass rod which passes through the centre. The plate is covered with a layer of cotton on which a similar porcelain plate is placed to prevent the cotton from floating. The funnel is inserted into a strong vacuum flask, which is connected with a Chapman air pump. Boiling water is first passed through the filter to warm it thoroughly, after which the agar is added and suction applied. As soon as the pump begins to act the top plate can be removed.

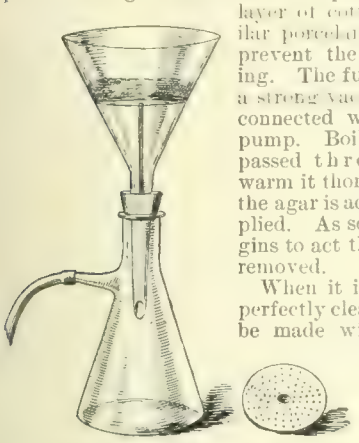

FIG. 5052. Filtration Through Cotton Over a Porcelain Plate. (Novy.)

When it is desired to make a perfectly clear medium it should be made with only one or one and a half per cent. of agar instead of two per cent., as given above. Such agar is softer and can be passed through a previously moistened filter paper, especially if the funnel is placed in a steam sterilizer or in a funnel shaped copper water bath, such as is shown in Figs. 5053 and 5054.

The filtered agar is then tubed and sterilized by steaming one-half hour on each of three consecutive days, after which it is kept in an upright position. When it is desired to make inclined or slant agar tubes, as many of these as are needed are melted in a water-bath and then inclined so that the agar comes within an inch of the cotton plug.

Thalmann's Agar.—Five hundred grams of meat are boiled for one-quarter of an hour with 1 000 c.c. of distilled water, after which the mass is made up to the original weight and strained through muslin. One per cent. of peptone and 0.5 per cent. of salt are then added, and the liquid is boiled, after which it is again made up to the original weight, cooled, and filtered. One and one-half per cent. agar is then added and the weighed liquid is boiled in a concentrated salt-water bath for about three-quarters of an hour, after which it is again made up to the original weight. Thirty cubic centimetres are then titrated with normal sodium hydrate, using phenolphthalein as an indicator. The amount of alkali necessary to neutralize the entire amount of agar is ascertained and two-thirds of this quantity is then added, in portions and while shaking, to the agar. After heating fifteen minutes the material is filled into tubes.

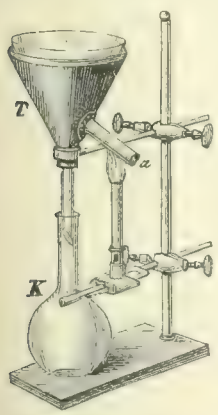

FIG. 5053. Double-Walled Hot-Water Funnel.

According to Thalmann and others this medium is adapted for the cultivation of the gonococcus, especially for diagnostic purposes. A little of the pus is mixed with the water of condensation, and then by means of a wire, rod, or cotton swab the suspension is thoroughly spread over the surface of a series of inclined tubes or over Petri dishes. These when kept for twenty-four hours at 36°–37° show small, glistening colonies, which are single or confluent and appear like highly refractive drops.

The medium is not suitable for subcultures, and Thalmann recommends that the colonies be transplanted to serum bouillon. This is prepared by adding to some bouillon two-thirds to three-fourths of the amount of alkali needed to neutralize the liquid. After heating and filtering, an equal volume of hog serum is added and the mixture tubed. The tubes are inclined and heated for one to two hours at 70° on the first and also on the second day, and for one hour at 100° on the third day. According to Wassermann hog serum is just as good as human serum for cultivating the gonococcus.

Glucose Agar.—This is made by adding to the filtered agar, or to so much of it as may be wanted, two per cent. of glucose. The medium is then tubed and sterilized in the ordinary way. It is used especially for the growth of yeasts and anaërobic bacteria. If desired it may be colored with litmus as in the case of gelatin.

Rothberger's Neutral-red Agar.—This can be made by adding to a 0.3 per-cent. glucose agar one per cent. of a saturated aqueous neutral red solution. The typhoid bacillus does not change the color or produce gas, whereas the colon discharges the red and leaves a fluorescing color. The inoculation can be made either by planting a shake culture or by making a stab culture, which can then be covered with a layer of agar to exclude air changes. The addition of neutral red to bouillon is of service in water examinations (Irons, Jordan).

Lactose Litmus Agar.—This medium was introduced by Wurtz, and is very useful in differentiating between the typhoid and colon bacilli. Acid formation in the case of the latter is indicated by a change in the reaction of the litmus. If this medium is made by the addition of two per cent. of lactose and litmus to the ordinary agar it will be found that even typhoid bacilli will give a slight acid reaction. This, however, is not due to the fermentation of the lactose, but to the small amounts of muscle sugar derived from the meat. It is therefore desirable that the agar for this purpose should be made out of sugar-free bouillon, which can be prepared according to the directions already given. Prolonged boiling of the agar must be avoided, inasmuch as the agar itself, since it is a complex carbohydrate, may split off some sugar.

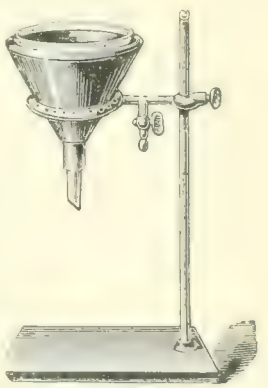

FIG. 5054. Single-Wall Hot-Water Funnel with Ring Burner.

It is often preferable to make the plain lactose agar and to add to the tubed and sterilized medium, whenever needed, by means of a sterile pipette, a sterile litmus solution. Obviously other indicators, such as rosolic acid, neutral red, etc., may be added in the same way.

Glycerin Agar.—To the ordinary nutrient agar prepared as above, five per cent. of glycerin is added. The addition of glycerin serves to keep the surface of the medium moist, and at the same time imparts nutritive qualities to the agar. This medium is very valuable for the growth of diphtheria, glanders, pneumonia, and tubercle bacilli.

Mannite Agar.—Mannite, which like glycerin is a polyatomic alcohol, was first used by Norris and Hiss as a means of differentiating the typhoid from the dysentery bacillus. The latter organism does not give rise to acid production when grown on mannite media, whereas the typhoid bacillus does. The agar should be prepared from sugar-free bouillon, and to it one or two per cent. of mannite is then added. Litmus may be added to the bulk medium before it is tubed, or the sterile litmus solution may be added to the sterile tubed agar by means of a pipette whenever needed.

Pfeiffer's Blood Agar.—This is made by spreading over the surface of ordinary inclined agar a few drops of human blood. On the surface thus prepared he was able to cultivate the influenza bacillus. The blood from the

lower animals can be used in like manner to good advantage.

The human blood required for this and similar purposes can be drawn without difficulty by means of a sterile syringe from the large median veins just below the flexure of the elbow. The superficial circulation should first be diminished by means of a rubber tube tied about the middle of the arm. The surface of the skin over the vein to be punctured is thoroughly cleaned by means of a disinfecting solution, such as mercuric chloride or lysol. The needle of the sterile syringe is then introduced into the vein, and as the piston is slowly withdrawn the syringe fills with blood. Five or ten cubic centimetres of blood can thus be obtained in a few minutes. When the needle is withdrawn a compress of cotton, soaked in mercuric chloride, should be applied to the wound. The blood must be at once transferred to either the surface of inclined agar or to previously melted agar, cooled to 50° C. In the latter case it is mixed at once, and the tube is then set aside in an inclined position to solidify.

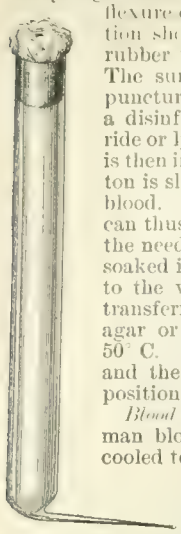

FIG. 5055.—Blood Pipette, Novy Form.

Blood Agar Mixture.—As just described human blood may be mixed with melted agar, cooled to 50° C., after which the mixture may be allowed to solidify in an inclined position. For diagnostic purposes this procedure has been utilized to detect the presence in the blood of typhoid bacilli, gonococci, and other organisms. Instead, however, of allowing the blood mixture to solidify in the tube it is poured out into a sterile Petri dish, and in this way a blood-agar plate is obtained, on which eventually colonies of the suspected organism may develop. The presence of a very few organisms can thus be detected in 1 or 2 c.c. of blood, which would not be possible by direct examination or by staining. The amount of blood which is added to the agar may be varied according to circumstances. Thus it may be one to four, one to two, or even one to one.

Blood from the lower animals can be drawn under strictly aseptic conditions into sterile Nuttall's blood pipettes, or into the modified form of Novy, shown in Fig. 5055. This can be easily made from test tubes of various sizes, according to the kind of animal to be bled. Thus a five-eighth by five-inch test tube may be used for bleeding a mouse or rat, while a one- by eight-inch tube would be used in the case of a rabbit. The bottom of the test tube and the end of a piece of glass tubing are softened in the flame of a blast lamp and then brought together. A narrow blast flame is then directed against the test tube about an inch from the bottom. On slow rotation in a horizontal position a thickened constriction results, and as soon as this is sufficiently thick the two ends are pushed apart slowly. A tapering capillary results, which is then sealed in the flame at a point about two inches from the tube proper. The tube is then plugged with cotton and sterilized by dry heat. When it is desired to prepare sterile defibrinated blood a drawn-out tube or a narrow glass rod is passed through the centre of the plug. By moving this about, after the blood has been received in the pipette, complete defibrination can be obtained, and that without any contamination from the outside.

In the case of the larger animals the blood is best drawn from the carotid artery. For this purpose the animal is anæsthetized and the artery exposed for about an inch. After the first incision it is advisable to avoid the use of cutting instruments, and instead to separate the tissues with the fingers. Pressure forceps are then applied at the distal end of the artery. Another pair are then applied about an inch below this point. A finger is then placed under the clamped portion of the artery and a very slight opening is made into the blood-vessel. The blades of a very narrow pointed pair of forceps are then introduced into the opening, and, when distended, the tip of the sterile blood pipette can readily be introduced. Before this is done, however, the tip should be scratched with a file, then broken off, and the open end should be flamed for a moment to insure sterility and to round off the sharp edge. As soon as the pipette is in position the lower clamp is removed, when the blood rapidly rises in the tube. If defibrinated blood is desired, the blood should be stirred by an assistant. When serum is wanted this stirring is omitted. As soon as blood ceases to flow, the pipette is removed and the tip is sealed in the blast lamp.

Obviously in the case of small animals, such as the mouse or rat, this procedure is not applicable. The blood may be drawn up into a syringe from the artery. A much better way, however, which has been used for several years in the author's laboratory, is to take the blood directly from the heart into a small pipette of the same form as that used for the larger animals. For this purpose the thorax is opened, the heart is freed from the pericardium and raised by means of oval-tipped forceps. The end of the pipette is then introduced into the right ventricle. Suction may be applied to the end of the pipette in order to obtain the fullest possible yield.

Blood can be drawn from very large animals, such as the horse, by introducing a trocar into the jugular vein. This is the procedure which is followed in the preparation of antitoxins. The trocar is connected by means of a short rubber tube with a glass tube, which is inserted into the receiving cylinder. In this way several litres of blood can be drawn from the horse at each bleeding.

In ordinary laboratory work the blood which has been collected in the glass pipettes is then transferred to melted agar, which has been previously cooled in the water-bath to 50° C. The amount of blood which is added to each tube will vary with the purpose in view. It may be one part of defibrinated blood to ten of agar, or one to five, one to two, or one to one, as the case may be. Exceptionally two to one and three to one are used. The blood is then mixed with the agar and the tubes are set aside to solidify in an inclined position. The transfer of the blood to the tubes is best accomplished by means of a sterile drawn-out bulb pipette, such as is shown in Fig. 5084, *e*.

The blood agar thus prepared requires no further sterilization, for if the operation has been properly carried out no organisms will be present. The tubes can be used for culture purposes at once, or they may be kept for several days to allow any organisms which might be present to develop. This blood medium is invaluable for the cultivation of various pathogenic organisms. On such media it has been possible, for example, to grow for the first time pathogenic protozoa—the trypanosoma Lewisi of rats and the trypanosoma Brucei, the cause of nagana or the tsetse fly disease (Novy and McNeal).

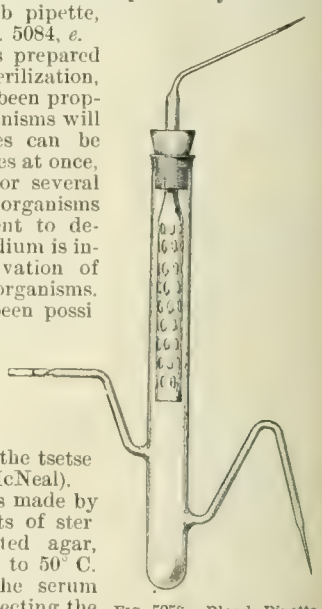

FIG. 5056.—Blood Pipette of Latapie.

Serum Agar.—This is made by adding variable amounts of sterile serum to the melted agar, which has been cooled to 50° C. in the water-bath. The serum can be obtained by collecting the blood, as given above, in sterile pipettes. The blood is allowed to clot, and eventually when the serum has separated it can be drawn up into sterile bulb pipettes and transferred to the melted agar. The largest yield of serum is obtained by using the Latapie pipette shown in Fig 5056. This consists of an inner tube, which is

freely perforated and the narrow, outer end of which is drawn out into a capillary for insertion into the blood-vessel. This tube is held in position within the outer one by means of a rubber stopper. The outer receiving tube, which is about an inch in diameter, is provided with two side tubes, one of which is drawn out and sealed while the other is plugged with cotton. The entire pipette is first sterilized by steaming in an autoclave. The tip of the inner tube is then broken, flamed, and inserted into the carotid artery of a rabbit or other animal. The blood should not fill the pipette beyond the inner tube. The tip is then sealed and the pipette is allowed to remain in a vertical position until the blood has firmly clotted. It is then inverted and the serum, as it is squeezed out of the clot, falls to the bottom. The purpose of the perforated inner tube is to allow more complete shrinking of the clot. The serum drains away at once from the clot, and is therefore perfectly clear. When it is desired to remove the serum the tip of the side tube is scratched with a file, then broken off, and the end is flamed to insure absence of bacteria. The tube is then inserted into a sterile test tube or flask and by blowing into the other side tube the serum is forced out. It can then be distributed to the agar tubes by means of a sterile bulb pipette. These are then allowed to solidify in an inclined position. As in the case of blood agar the medium prepared in this way is perfectly sterile, if the manipulation is properly carried out. Inasmuch as sterilization by heat is avoided, the proteid constituents of the serum remain in as near to the native condition as possible. Such serum agar makes an excellent medium for the pneumococcus and for other organisms. Obviously, serum-agar plates can be prepared, if it is so desired, in which case the melted and cooled agar is inoculated with the organism to be cultivated, after which the serum is added and mixed with the agar, which is then poured out into sterile Petri dishes.

Serum agar, made by adding human blood serum to melted agar, has been used for the cultivation of the gonococcus (Wertheimer). Ascitic or pleuritic fluid may also be added to agar in the proportion of one part of the fluid to two parts of the agar. Such agar is used especially for the cultivation of the gonococcus. The ascitic, pleuritic, or hydrocele fluids may be sterilized by fractional sterilization or by filtration through a Berkefeld filter under pressure.

Wassermann's Serum-Nutrose Agar.—This also has been found useful for cultivating the gonococcus. Five cubic centimetres of hog serum are added to 30 to 35 c.c. of water, 2–3 c.c. of glycerin, and 0.8–0.9 gm. of nutrose. Nutrose is a sodium phosphate casein compound, and when added to serum prevents coagulation on boiling. The solution is boiled for twenty minutes, after which it is added in equal parts to two per cent. peptone agar in test tubes. This mixture is then poured into Petri dishes. Nutrose has been used also in the preparation of the Drigalski-Conradi agar. Hog serum, which is said to be as good as human serum for cultivating the gonococcus, has been employed also by Thalmann.

Drigalski and Conradi Agar.—This is a meat-peptone-nutrose agar containing lactose, litmus, and crystal violet. The preparation is as follows: 1. A mixture of three pounds of meat and two litres of water is allowed to stand for twenty-four hours; the expressed meat juice is then boiled for one hour and filtered. To the filtrate are added 20 gm. of Witte's peptone, 20 gm. of nutrose, 10 gm. of sodium chloride, and the whole is boiled for one hour and filtered. To this filtrate 60 gm. of agar are added and the liquid is boiled for three hours, or one hour in an autoclave. It is then rendered alkaline to litmus paper, boiled half an hour, and filtered. 2. A solution of litmus is prepared according to Kubel-Tiemann as follows: The powdered commercial litmus is repeatedly extracted with hot distilled water. The liquid is acidulated with dilute acetic acid and evaporated to syrupy consistence on a water-bath. The thick fluid is then diluted by the gradual addition of ninety-per-cent. alcohol, transferred to a flask, and an excess of ninety-per-cent. alcohol is added. This precipitates the blue pigment, while the red dye and the potassium acetate remain in solution. The precipitate is filtered and washed with alcohol, then dissolved in distilled water, after which the solution is warmed and filtered. The filtrate is then added gradually to very dilute sulphuric acid (one or two drops of acid to 200 c.c. of water) till the color changes to a wine red. The concentrated blue is then added till the blue color is restored; 260 c.c. of this litmus solution are boiled for ten minutes, then 30 gm. of pure lactose are added, and the boiling is continued for fifteen minutes. 3. The hot litmus is added to the hot agar, mixed, and the reaction is made slightly alkaline; 4 c.c. of a hot sterile solution of ten-per-cent. anhydrous soda and 20 c.c. of a freshly prepared solution of 0.1 gm. of crystal violet in 100 c.c. of warm sterile water are then added, after which the material is filled into tubes or flasks. Excessive heating should be avoided, inasmuch as it alters the lactose. The crystal violet is intended to restrict the development of the unimportant bacteria.

The Drigalski-Conradi medium has been recommended for the isolation of the typhoid bacillus. For this purpose the fæces should be diluted with ten to twenty volumes of salt solution. The authors employ large plates, 15–20 cm. in diameter. The agar is poured into the dishes to a depth of at least 2 mm., and the cover is then kept off till the moisture has dried off the surface of the agar. By means of a 5 mm. glass rod, bent at right angles and previously dipped in the suspension, a series of streaks are made over a number of the dishes. The inoculated plates are then kept at 37° C. for twenty-four hours. The colon colonies are large, opaque, and red, while the typhoid are small, glassy, and resemble dew drops. The further identification of the suspected colony is made by applying the agglutination test and by growing in Rothberger's neutral red agar.

Gelatin Agar.—Several formulas have been proposed for the preparation of this medium. Each finds its special application. That of Capaldi was recommended for the isolation of the typhoid bacillus from fæces. It is made by dissolving 20 gm. of Witte's peptone, 10 gm. of gelatin, 10 gm. of glucose or of mannite, 5 gm. of sodium chloride, and 5 gm. of potassium chloride in 1,000 c.c. of water. The solution is filtered and two per cent. of agar is added and dissolved by boiling, after which it is rendered alkaline by the addition of 10 c.c. of normal alkali. The filtered solution is then tubed and sterilized by steaming.

Stoddart's medium is a gelatin agar which contains five per cent. of gelatin, one per cent. of peptone, and a half per cent. each of agar and of salt. A litre of meat extract is prepared in the usual way. In this 10 gm. of peptone and 5 gm. of salt are dissolved, and the solution is then divided into two parts. To one portion ten per cent. of gelatin is added, and when this has dissolved, the solution is neutralized and an excess of 10 c.c. of normal alkali per litre is added. The other half of the meat extract is likewise neutralized, and then 10 c.c. of the normal alkali are added per litre to impart the requisite reaction. The liquid is then measured or weighed, boiled, and filtered. Five grams of cut agar are added to the bouillon, which is then boiled until the agar dissolves. Distilled water is added to make up to the original volume or weight, after which the two liquids are combined and allowed to sediment. The entire product is finally filtered through cotton or, better, through paper. The medium is filled into tubes which are then steamed for fifteen minutes on each of three consecutive days. To use this medium, it is poured out into sterile Petri dishes, and when solidified the centre is touched with the organism to be tested. The typhoid bacillus, on account of its motility, spreads rapidly over the surface as an almost transparent growth, whereas that of the colon bacillus spreads less and is easily visible.

Guarnieri's gelatin agar is made in a somewhat similar

manner. Three grams of powdered agar are emulsified with 50 c.c. of distilled water, and this is then added to a solution of 50 gm. of gelatin in 750 c.c. of meat extract. The whole is boiled till the agar has dissolved, when a solution of 25 gm. of Witte's peptone and 5 gm. of salt are added. The entire liquid, which now makes up to one litre, is then carefully neutralized with normal alkali, using litmus as an indicator. The medium is tubed and sterilized as usual. It has been used to advantage in the cultivation of the pneumococcus.

Weil's Meat Potato Agar.—The potato juice is prepared as in the method of Holz or Elsner; 300 c.c. of this are added to 200 c.c. of slightly alkaline bouillon; 3.75 gm. of agar are then dissolved in the liquid, thus yielding a 0.75-per-cent. agar solution. The typhoid bacillus presents threaded colonies on this medium, the same as in Elsner, Hiss, and Piorkowski media.

Substitutes for the Meat Infusion.—In the preparation of the foregoing media a meat infusion served as the basis in each case. In special instances, but not as routine procedure, these media may be modified by using the commercial Liebig's beef extract in place of the meat infusion. The chief advantage lies in the fact that the beef extract can be kept always on hand. At the same time it must be remembered that media made up with such extract are by no means as nutritious as those made up with the meat infusion. The amount of Liebig's extract which is used varies with different workers. In general, from 1 to 3 gm. are added to one litre of water; 5 and even 10 gm. are also used. To this solution peptone and salt may be added in the usual amounts. The liquid when rendered alkaline and filtered constitutes a Liebig's extract bouillon. In the same way gelatin and agar media are prepared.

Peptone Substitutes.—Several compounds have been suggested as substitutes for Witte's peptone. In Martin's and Peckham's bouillon and in Deycke's agar this peptone is replaced by that which is formed by the digestion of the muscle tissue. In other media derivatives of albumen or casein are employed. Heyden's "Nährstoff" is a digested egg albuminate, while nutrose is a casein compound. The addition of lecithin, protogen, and hæmoglobin, etc., is made with the object of improving the nutritive qualities of the media.

Hiss' Tube Medium.—This is used as a means of testing for the typhoid bacillus. It is made by adding 5 gm. of Liebig's extract, 5 gm. of salt, and 5 gm. of agar to 1,000 c.c. of water. The mixture is then heated until the agar has dissolved, after which the water which is lost by evaporation is replaced and then eight per cent. gelatin is added. As soon as the gelatin has dissolved, the liquid is partially neutralized by the addition of normal alkali. The reaction is left acid, and to such an extent that it would require 15 c.c. of normal alkali per litre to make the solution neutral to phenolphthalein. The liquid is then cooled to 60° C. and cleared by the addition of the white of an egg stirred up in about 25 c.c. of water. The liquid is then boiled for a few minutes, after which 10 gm. of glucose are added. After sedimentation at 50° C. the medium can be filtered through paper or cotton and tubed. This medium is used only for stab cultures. Diffusion of the growth through the medium in the case of very motile organisms, such as the typhoid bacillus and the production or absence of gas, are the criteria sought for.

Hiss' Plate Medium.—Hiss utilized the tendency of the typhoid bacillus to form threaded colonies when grown on soft media, as a means of differentiation from the colon bacillus. The medium, as first proposed, contained 15 gm. of agar, 15 gm. of gelatin, 5 gm. each of Liebig's extract and of sodium chloride, 10 gm. of dextrose, and 1,000 c.c. of distilled water. This was cleared by the addition of the whites of two eggs and filtered through absorbent cotton. The reaction was left acid, and of such extent that it would require the addition of 2 c.c. of normal alkali to make it neutral to phenolphthalein. Subsequently Hiss made various modifications of this formula, eliminating the unnecessary constituents. The simplest combination, which was found to give excellent results, was made by adding 15 gm. of agar and 5 gm. of Liebig's extract to 1,000 c.c. of distilled water. No acid or alkali was added. The medium was cleared by the whites of two eggs and filtered through cotton. Plate cultures, made at 37° C., show excellent differentiation between the colonies of typhoid and colon bacilli in twenty-four hours. The former show threaded colonies, the latter do not.

Hesse's Nährstoff-Heyden Agar.—The "Nährstoff-Heyden" is an albumose made from egg albumen. It should first be stirred up in a beaker with a little water, and then added to the liquid. For cultivating the tubercle bacillus the medium consists of: 5 gm. Nährstoff-Heyden, 5 gm. salt, 30 gm. glycerin, 10 gm. agar, and 1,000 c.c. of distilled water; 5 c.c. of normal soda solution are added. The latter represents a 14.3 per cent. of the crystalline salt ($Na_2CO_3 + 10\ H_2O$) and not 28.6 per cent., as stated by Hesse. The Hesse-Niedner agar, which has been recommended for the study of water bacteria, is made by dissolving 7.5 gm. of Nährstoff-Heyden and 12.5 gm. of agar in 1,000 c.c. of distilled water. Gage and Phelps dissolved one per cent. each of agar and of the Nährstoff in 1,000 c.c. of distilled water, and made the solution neutral to phenolphthalein.

Blood Serum.—The preparation of serum from small animals has been described at length under serum agar. When it is desirable to use large quantities of serum it is advisable to collect ox blood at a slaughter-house. The more care taken in collecting the blood under aseptic conditions the less troublesome will be the subsequent sterilization. A convenient receptacle is a half-gallon battery jar covered with paper and previously sterilized. The spurting blood is received directly into the jar, after which the paper cap is replaced and the blood set aside until it firmly clots. It can then be transported to the laboratory and set aside in a cool place for the serum to separate. The serum can then be drawn up by means of an aspirator into a sterile globe receiver, such as is shown as a part of Fig. 5060. It can then be conveniently filled into test tubes or into flasks.

The earliest method of sterilizing blood serum is that of Koch by fractional heating. The tubes were placed in an inclined position in a serum coagulator shown in Fig. 5057. The Roux water bath, shown in Fig. 5063, is particularly useful for this purpose. The serum tubes are immersed in the water at 58° C. The serum tubes are heated for an hour at 58° C. on each of seven successive days. This low temperature is selected in order to accomplish the sterilization and yet keep the serum in a

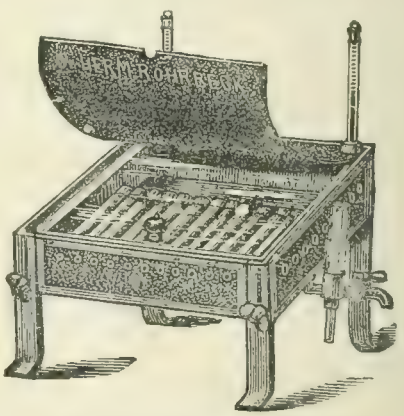

FIG. 5057. Koch's Blood Serum Coagulator.

fluid condition. Unfortunately bacteria may be present in the serum which will actually grow at the temperature employed, and in that case this method of sterilization is inapplicable. Some have endeavored to obviate this difficulty by filtering the serum through a Berkefeld

bougie. Martin suggested that one to two per cent. of chloroform be added to the serum, which is then set aside for several months, after which the chloroform can be driven off by heating at 65°. Fraenkel dispensed with the sterilization, relying entirely upon the aseptic collection of the serum. When the serum is collected with the care outlined above, it will be found that very few bacteria are present. Consequently after the tubes have been filled with the serum they may be incubated for several days, and at the end of that time the contaminated ones can be discarded. This procedure is preferable to those just given. The sterile serum is then coagulated in an inclined position by raising the temperature of the sterilizer to 65° C., and keeping it there until the serum has become solid. The medium thus prepared is transparent and solid. When a higher temperature is used the serum coagulates to an opaque white mass.

Inasmuch as the above methods require much time and skill and are in themselves very tedious, they have been largely supplanted by fractional sterilization in steam. For this purpose the tubes are first placed in an inclined position, either in a dry-heat oven, or, better, in the coagulator, and then heated to 85° to 95° C. until firm coagulation results. If this is not looked after the medium will be torn up by gas bubbles during the next step. The coagulated serum tubes are then placed in wire baskets and steamed, as in the case of agar, for half an hour on each of three consecutive days. The medium thus prepared is fully as useful as that which is transparent.

Löffler's Blood Serum.—This consists of one part of a one-per-cent. glucose bouillon and of three parts of blood serum. This mixture is filled into tubes and sterilized in the manner just given. It is used very extensively for the diagnosis of diphtheria.

Glycerin Serum.—Five per cent. or more of glycerin is added as in the case of glycerin agar. The sterilization is the same as that just given. It is used for the cultivation of the tubercle bacillus.

Serum Water Media.—When serum is diluted with five to ten parts of water it can be sterilized by steaming without coagulation taking place. Hiss employed such a medium in differentiating between the pneumococcus and streptococcus; also in distinguishing between the dysentery and allied organisms. He prepares the medium by adding one part of clear beef serum to two parts of distilled water. The mixture is first heated to 100° for a short time, so as to destroy the glycolytic enzyme which is present, after which one per cent. of the sugar desired is added. Dextrose, galactose, mannite, maltose, lactose, saccharose, inulin, and dextrin have been thus used. The medium is colored by the addition of one per cent. of a five-per-cent. aqueous litmus solution. The medium is then tubed and steamed for ten minutes on three consecutive days.

Marmorek's Media.—In order to maintain streptococci at their maximum virulence Marmorek used several media, preference being given to them in the following order:

1. Human serum 2 parts, bouillon 1 part.
2. Pleuritic or ascitic fluid 1 part, bouillon 2 parts.
3. Serum of mule or ass 2 parts, bouillon 1 part.
4. Horse serum 2 parts, bouillon 1 part.

These media can be sterilized by fractional heating at low temperature, or, better, by filtration through a Berkefeld bougie.

Thalmann's serum bouillon for cultivating the gonococcus has been mentioned in connection with his agar.

Milk.—This is an excellent medium for diagnostic purposes. It is advisable to use centrifugated milk if possible. Otherwise the whole milk is placed in a beaker or flask and steamed for about half an hour. When partially cooled it can be poured into a large separatory funnel, or into a bulb receiver shown as part of Fig. 5060, and allowed to stand thus overnight. The underlying layer of fat-free milk can then be filled directly into tubes. These are then sterilized by steaming half an hour on each of three consecutive days. When time is an object the whole milk may be filled directly into tubes. If desired the milk may be colored with litmus. Instead of milk, whey may be used to good advantage. This can be prepared by coagulating the milk with rennet. The liquid is first separated by means of cheese-cloth and finally put through paper. It is then colored with litmus, filled into tubes, and sterilized. Care must be taken not to overheat the milk lest the lactose undergo more or less oxidation. Whey-gelatin and whey-agar are used for special purposes.

Urine.—By discarding the first portion of urine which is passed the remainder can be collected in sterile flasks and will be free from bacteria. Such urine may be used directly for studying the various fermentations which it may undergo. To prepare a urine gelatin the secretion should be diluted so as to have a specific gravity not to exceed 1.010. Ten per cent. of gelatin is then added, and when it has dissolved the reaction is made to correspond to that of the original urine. Heller's urine gelatin is prepared in the same way, but has one per cent. peptone and a half per cent. of salt. After solution the liquid is rendered faintly alkaline, then filtered and tubed.

Piorkowski Urine Gelatin.—Normal urine of 1.020 specific gravity is collected for two days, and is allowed to become slightly alkaline in reaction. Then 1.5 per cent. peptone and 3.3 per cent. gelatin are added, and the mixture is heated for one hour on the water-bath, after which it is filtered and filled into tubes. These are sterilized by heating for fifteen minutes at 100° on the first day, and for ten minutes on the second day. The medium is used to differentiate the typhoid from the colon bacillus. Petri plates are made and developed at 22° C. for twenty-four hours. While the colon colonies are roundish, finely granular, sharp-bordered, and yellowish, the typhoid colonies are small and show a more or less marked threaded border. This method has given good results in connection with the examination of typhoid fæces.

Urine Agar.—This can be prepared by adding to the freshly passed urine two per cent. of finely cut agar. The mixture is then boiled until solution results, when it is filtered through cotton or paper as in the case of ordinary agar. This agar is then filled into tubes and sterilized by steaming.

Another way of preparing a urine agar is to collect the urine, after discarding the first portion which is passed, in a sterile flask, and then to transfer it by means of a pipette, as in the case of blood or serum, to the melted and cooled agar. One part of urine to two parts of agar is ordinarily used. Normal or albuminous urine may be used for this purpose, and with very little care the urine can be collected entirely free from bacteria. Such urine agar has been used to advantage for growing the gonococcus.

Internal Organs.—For special use the several media, such as bouillon, agar, and gelatin, may be made up with the finely divided organs in place of the minced meat. At times the solid organs are sterilized and used as such. The steamed brain, for example, when cut up into slices and sterilized, can be used for cultivating the tubercle bacillus (Ficker); and also the gonococcus (Thalmann).

Egg Media.—Hueppe first suggested the use of fresh eggs as a culture medium. For this purpose the shell is thoroughly cleaned and disinfected with mercuric chloride. A small opening is then punched through the shell, and through this the organism to be tested is introduced into the inside. The opening is then sealed with a bit of sterile paper and collodion. Another procedure is to insert through the opening in the shell a rather wide, drawn-out tube pipette. On applying suction, especially with the aid of an aspirator, the contents of the egg can be drawn up into the bulb, and can then be distributed to tubes (Novy).

The egg may be used as a solid opaque medium according to Wesener. The egg is thoroughly agitated so as to mix the yolk with the albumen. It is then coagu-

lated at 75 to 80° C., after which the shell is removed and the contents are cut up into slices and placed in suitable dishes and sterilized by steam. In like manner the coagulated white of the egg may be cut up into slices and tubed. A transparent, coagulated egg albumen may be prepared by converting it into an alkali albuminate, as suggested by Tarchanow and by Karlinski. For this purpose the egg is placed in ten-per-cent. potash for fourteen days, after which the shell is removed and the solidified egg is cut up into slices, tubed, and sterilized.

Potatoes.—These may be prepared in several ways. The old method, introduced by Koch, is still used where mass cultures are desired. The potatoes are scrubbed clean under the tap, and any bad spots carefully removed by means of a knife. They are then placed in boiling water or steamed for three-quarters of an hour. By means of a knife, which has been sterilized in a flame, they are then cut into halves and placed in a large moist chamber or suitable pan provided with a lid. The bottom of this vessel should first be covered with a piece of filter paper which has been moistened with water or with mercuric chloride. The cut and sterile surface of the potatoes can then be inoculated with the organisms to be cultivated, either by spreading the material over the potato with a sterile knife or by making parallel streaks. Inasmuch as there are several sources of contamination in this method, it has been largely displaced by the modified procedures.

In Esmarch's modification the potato is pared and cut into slices about a third of an inch thick, after which they are placed into small glass dishes about 7 cm. in diameter and 1 cm. high, known as Esmarch dishes. These are then sterilized by steaming in the usual way.

The best way of using potatoes for culture purposes is that introduced independently by Bolton and Globig. The cleaned potato is placed in boiling water for about half an hour. By means of a cork borer or a test tube, the end of which has been cut off, cylinders of potato may be punched out. The skin is removed from the ends of the cylinders, after which these are halved by a diagonal cut. The wedge-shaped semicylinders are now placed in sterile test tubes and sterilized by steam.

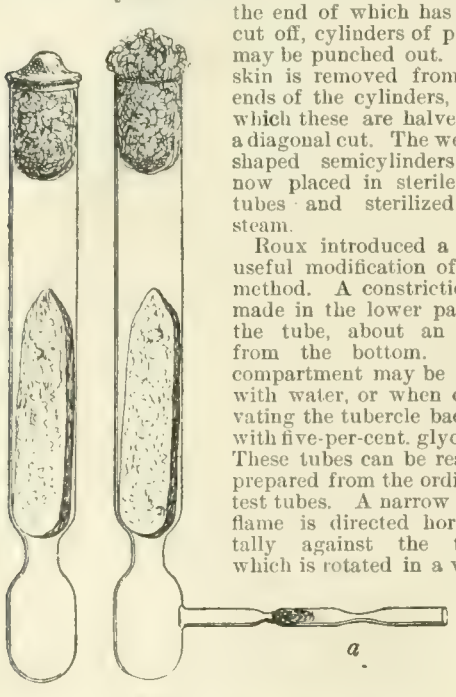

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FIG. 5058. Roux Tube for Potato Culture.

Roux introduced a very useful modification of this method. A constriction is made in the lower part of the tube, about an inch from the bottom. This compartment may be filled with water, or when cultivating the tubercle bacillus with five-per-cent. glycerin. These tubes can be readily prepared from the ordinary test tubes. A narrow blast flame is directed horizontally against the tube, which is rotated in a vertical position. The Roux tube is shown in Fig. 5058. A good substitute for this tube may be made by placing on the bottom of the test tube a layer of absorbent cotton, which may be soaked with the glycerin solution.

Mashed potatoes spread over the bottom of a flask have been used, but they offer no special advantage over the methods given. The preparation of potato gelatin with or without potassium iodide has already been described

Bread Medium.—Ordinary bread is toasted to a crisp, then powdered, in which condition it may be kept in stock. For use the powder is placed on the bottom of small flasks and thoroughly moistened with water, then sterilized by steaming. This medium is particularly useful for cultivating moulds.

Plant Infusions.—These are useful for growing certain bacteria and also amœbæ. Infusions of hay, straw, fruits, grains, etc., take the place of meat extract. By the addition of agar or gelatin solid media may be prepared. Beer wort, either as such or as a gelatin, is valuable for the cultivation of yeasts.

Proteid-free Media.—With the exception of urine all the media described thus far contain some proteid matter. The latter, however, is not essential, for it is possible to grow bacteria on media which contain sulphur, nitrogen, and phosphorus in inorganic combination. Such a solution was used, for instance, at a very early date by Pasteur. It consisted of 1 part of ammonium tartrate, 10 parts of candy sugar, the ash of 1 part of yeast, and 100 parts of water. The botanist Cohn employed a similar solution, consisting of 0.1 gm. each of potassium phosphate and magnesium sulphate, 0.01 gm. of tribasic calcium phosphate, 0.2 gm. of ammonium tartrate, and 20 c.c. of distilled water. Naegeli's solution was made by adding 1 gm dibasic phosphate, 0.2 gm. magnesium sulphate, 0.1 gm. calcium chloride, and 10 gm. of ammonium tartrate to 1,000 c.c. of distilled water.

After the lapse of many years these non-albuminous fluids were again brought into use in a modified form by Uschinsky. His solution consisted of: Water, 1,000 parts; glycerin, 30–40 parts; sodium chloride, 5–7 parts; calcium chloride, 0.1 part; magnesium sulphate, 0.2–0.4 part; dipotassium phosphate, 2–2.5 parts; ammonium lactate, 6–7 parts; sodium asparaginate, 3–4 parts.

Fraenkel's modification of this solution contains 5 gm. of sodium chloride, 2 gm. of potassium diphosphate, 6 gm. of ammonium lactate, and 4 gm. of sodium asparaginate. These substances are dissolved in 1,000 c.c. of water and the solution is then rendered slightly alkaline.

Similar solutions have been used by Maassen and by others. Thus Proskauer and Beck cultivated the tubercle bacillus on the following solution: Commercial ammonium carbonate, 0.35 per cent.; monopotassium phosphate, 0.15 per cent.; magnesium phosphate, 0.25 per cent.; glycerin, 1.5 per cent.

For cultivating the nitrous and nitric acid organisms Winogradsky employed wholly inorganic solutions. The nitric-acid producers were grown in a solution consisting of 1,000 c.c. of water, 1 gm. potassium phosphate, 0.5 gm. magnesium sulphate, 0.01 gm. calcium chloride, 2 gm. sodium chloride. This is filled into flasks in portions of 20 c.c. each, together with a little freshly washed magnesium carbonate. To these flasks, after sterilization by steam, 2 c.c. of a two-per-cent. solution of ammonium sulphate is added, after which they are incubated to eliminate contaminations.

For the nitrous-acid organisms the solution consists of 1 gm. ammonium sulphate, 1 gm. potassium sulphate, and 1,000 c.c. of water. It is filled into flasks, magnesium carbonate added, after which they are sterilized by steam.

As a substitute for gelatin Winogradsky employed silicic-acid jelly, which was added to solutions of essentially the same composition as those just given.

Standardization of Media.—The procedure as introduced by Koch, and still followed in many laboratories, is to add a saturated solution of sodium carbonate, in portions of a cubic centimetre or more, to the nutrient medium, to be neutralized until a drop of the mixture, transferred by means of a glass rod, turns red litmus paper promptly blue. In some laboratories a strong solution of sodium hydrate is used in the same way. Obviously this method lacks quantitative precision, and the

duplication of the same reaction in several batches of material is out of question. Moreover, it is an established fact that the reaction of a medium has a very important influence upon the development of bacteria. For these reasons the bacteriological committee of the American Public Health Association, adopting Fuller's work, recommended the following method for the titration of nutrient media. The reagents necessary are:

1. Five-tenths-per-cent. solution of phenolphthalein in fifty-per-cent. alcohol.
2. Normal sodium hydrate (N. NaOH). A litre of this solution contains 40 gm. of NaOH.
3. Twentieth normal sodium hydrate ($\frac{n}{20}$ NaOH). A litre of this solution contains 2 gm. of NaOH.
4. Normal hydrochloric acid (N. HCl). A litre of this contains 36.5 gm. HCl.
5. Twentieth normal hydrochloric acid ($\frac{n}{20}$). A litre of this contains 1.825 gm. of HCl.

The preparation of these solutions requires some familiarity with the methods of quantitative analysis. The solutions can be built up by starting from a twentieth normal solution of oxalic acid, or, better, succinic acid.

The titration is carried out as follows: To 5 c.c. of the filtered medium in a six-inch porcelain evaporating dish add 45 c.c. of distilled water and 1 c.c. of the phenolphthalein solution; boil for three minutes to expel carbonic acid, then run in the twentieth normal alkali, drop by drop, with constant stirring, until a bright pink color results. The number of cubic centimetres of the twentieth alkali required to neutralize 5 c.c. of the medium gives directly the number of cubic centimetres of normal alkali (*i.e.*, percentage) required by 100 c.c. of the medium. Thus if 5 c.c. of the medium requires 2.8 c.c. of $\frac{n}{20}$ alkali, then 100 c.c. would need 56 c.c. $\frac{n}{20}$, or 2.8 c.c. of N NaOH.

The quantity of the medium remaining is now measured and the amount of alkali needed for neutralization is calculated and added. After the addition of the alkali the liquid is boiled and a portion is then titrated as before. It should be neutral, and if it is not, as often is the case on account of unknown changes, the requisite amount of alkali to make it so is added to the bulk.

The medium which is neutral with reference to phenolphthalein is very alkaline with respect to litmus. Thus a bouillon which is neutral to litmus will require about 25 c.c. of normal alkali per litre to make it neutral to phenolphthalein. In general the addition of 10 c.c. of normal alkali to a medium which is neutral to litmus imparts the most favorable degree of alkalinity. Hence the optimum reaction with reference to phenolphthalein is obtained by adding 15 c.c. of normal acid to the litre of neutralized medium. It is customary to use the sign + to indicate an acid reaction, and that of − for one that is alkaline. Thus +15 means that the reaction is acid with respect to phenolphthalein, and that one litre of the medium would require 15 c.c. of normal alkali for neutralization.

The titration with litmus as an indicator is best carried out in the following way: Portions of 5 c.c. of the medium are measured out into each of four or five large test tubes. In the case of bouillon the amount of $\frac{n}{10}$ alkali needed to neutralize this amount may vary from 0.3 to 0.6 c.c. Hence to tube 1 add 0.3 c.c.; to tube 2 add 0.4 c.c.; to tube 3 add 0.5 c.c., etc. The contents of each tube are then boiled for a minute, after which a slip of red and of blue litmus paper is dropped into the hot liquid and allowed to remain there for about a minute. The papers are then drawn out, side by side, on the walls of the tube when the colors can be compared. In this way the amount of alkali necessary to neutralize 5 c.c. with respect to litmus can be determined. Bouillon, as well as agar, usually requires about 5 c.c. per litre for neutralization, while gelatin needs about 30–35 c.c. Having determined the amount needed for neutralization, this amount, together with an excess of 10 c.c. per litre, to impart a suitable alkaline reaction, is then added to the medium.

For ordinary purposes it is hardly necessary to resort to these rather complicated methods. It is sufficient to add directly to bouillon and to agar 15 c.c. of normal alkali per litre. Gelatin will require about 40 c.c. In general sodium carbonate is preferable to the hydrate

Preparation and Filling of Tubes.—The cheaper grades of test tubes should be avoided. They are very thin and therefore break easily, and, moreover, on heating they will often frost because of the separation of silicic acid. The best test tubes are the "blue-lined" or "resistant glass" quality, or those of genuine Bohemian glass. The size used varies with the purpose and the individual taste; 12 × 125, 15 × 150, and 20 × 150 mm. are convenient.

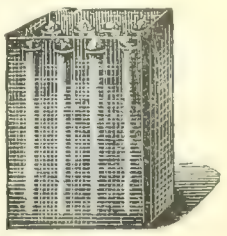


Fig. 5059. Wire Basket for Sterilizing Tubes.

The new tubes of the better glass can be used after being swabbed out with warm water.

The cheaper grades are very alkaline, and for that reason should be first soaked in very dilute warm hydrochloric acid, after which they should be rinsed or swabbed thoroughly in clean warm water. The cleaned tubes are allowed to drain, and when dry are plugged. Used tubes should be sterilized by steaming for a half-hour, after which they may be filled with water and again heated, so as to bring the more or less dried contents into solution.

The simplest way of plugging is to place over the mouth of the tube a piece of cotton, about two inches square, which is then pushed within by means of a narrow glass rod or a pair of smooth forceps. Such plugs answer all ordinary purposes. They are, however, rather loose, and permit evaporation of the media, and cannot be used where the tubes are to be sealed with wax. A firm solid plug is made by taking a piece of cotton, about three inches square. This is folded into thirds and then rolled up from the end into as firm a cylinder as possible. By a twisting motion the plug is inserted into the tube, and only enough cotton is left on the outside to permit grasping of the plug. The plugged tubes are then placed in a wire basket, such as is shown in Fig. 5059. These baskets are made of heavy galvanized netting. The usual size is 24 cm. high and 18 cm. square. Smaller baskets, 10 × 12 and 18 cm. high, are very useful. Circular baskets, of a size to fit the sterilizer, are also used.

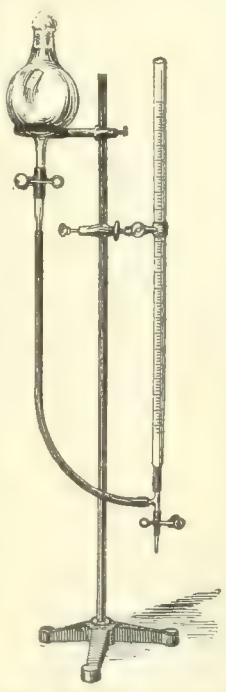


Fig. 5060. Globe Receiver for Filling Media into Tubes, with Burette Attachment. (Novy.)

Flasks, bulbs, etc., should be prepared for sterilization in the same way.

After the tubes have been sterilized by heating in the dry-heat oven they are ready to be filled with the nutrient media. This can be done by the aid of a small funnel. Where large quantities of media are to be tubed much time can be saved by using a large funnel or globe receiver, such as is shown in Fig. 5060. The lower end of the bulb is connected with a drawn-out glass tube and is provided with a pinch cock. In this way the media can be rapidly filled into the tubes. Ordinarily the tubes are filled to the depth of one and one-half or two inches. In special cases in which definite quantities are desired, the simple apparatus, shown in

Fig. 5060, can be used. The containers, with the media to be filled, can first be sterilized by steaming, after which the media can be measured out into sterile tubes, which will not require further treatment. A less desirable apparatus is that of Treskow, shown in Fig. 5061.

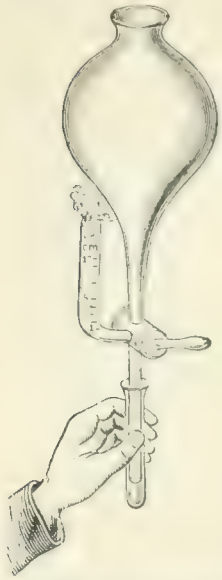


Fig. 5061.—Treskow's Apparatus for Measuring Media into Tubes.

Sterilization.—By sterilization is meant the total destruction or removal of all organisms in or about a given object. This can be accomplished in a variety of ways.

1. *By Direct Flaming.*—This method is applicable for the sterilization of glass rods, slides, cover-glasses, platinum wires, searing irons, and rough instruments. Valuable surgical instruments would of course be damaged by this procedure.

2. *By Means of the Dry-Heat Sterilizer.*—The form most often used is that of Koch, shown in Fig. 5062. This is made of sheet iron, is double walled, and the outer wall may be lined to advantage with thick asbestos board. The form as shown is designed to sterilize not only tubes and flasks but also glass tubing, pipettes, and the like. The oven is used for sterilizing only glass and metal ware. It must not be used for sterilizing media. A temperature of 150° C. should be maintained for one hour. Usually it will be sufficient to allow the temperature to rise, and as soon as it has reached 200° the gas is turned off. The cotton should show a slight tinge of yellow after this heating. If the plug browns considerably and powders it is due more to the fact that the cotton has been chemically treated than to the heat.

3. *Fractional Sterilization at* 56°–58° C.—This method was introduced by Tyndall, and has been used for the sterilization of liquid serum, milk, and other fluids which are liable to be altered more or less by heat. It is based upon the fact that the actively vegetating forms of bacteria are readily destroyed as a rule by exposure for some minutes to this temperature. The resting forms or spores are not in the least affected by such exposure. It is necessary to wait until the spores have germinated into the vegetating forms, which can then be destroyed by a second like heating. As ordinarily practised, the method is as follows: The tubes are placed in an apparatus, such as that shown in Fig. 5063, and are heated for one hour at the given temperature on each of seven or eight consecutive days.

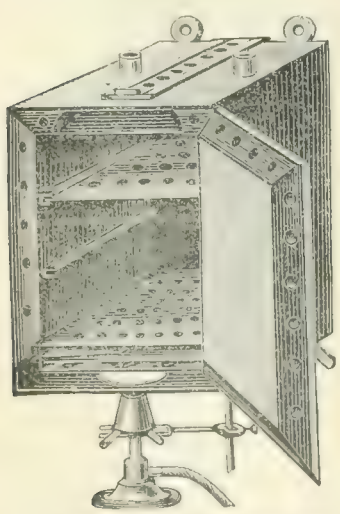


Fig. 5062. Koch's Dry-Heat Sterilizer.

This method sometimes gives good results, at other times it fails. The reason for this lies in the presence or absence of the so-called thermophilic bacteria. These organisms actually grow best at the temperature employed, and hence, if they chance to be present, the method is inapplicable. A temperature of 70° C. may be used in like manner, but this causes coagulation of the serum.

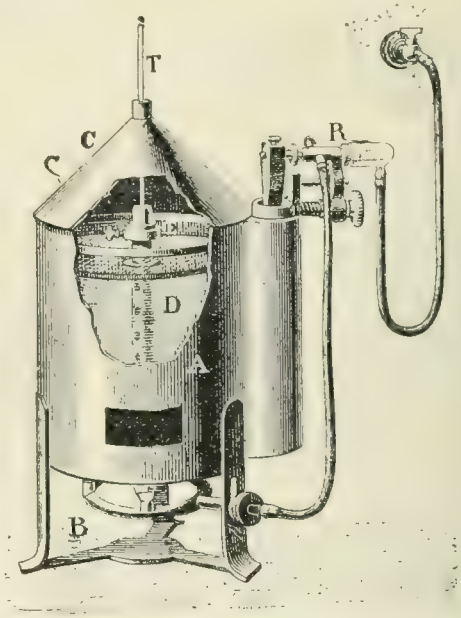


Fig. 5063.—Roux Water-Bath for Sterilizing Serum with Metallic Regulator.

By Pasteurization is meant the partial destruction of the organisms which are present in a milk. This is accomplished by exposing the milk for half an hour, or more, to a temperature of about 68° C. (155° F.). While this temperature does not destroy the spores which may be present, it does kill the lactic-acid and other bacteria, which do not produce spores. As a result, milk treated in this way will keep for several days without coagulating. If a higher temperature is used, the taste of the milk is likely to be impaired.

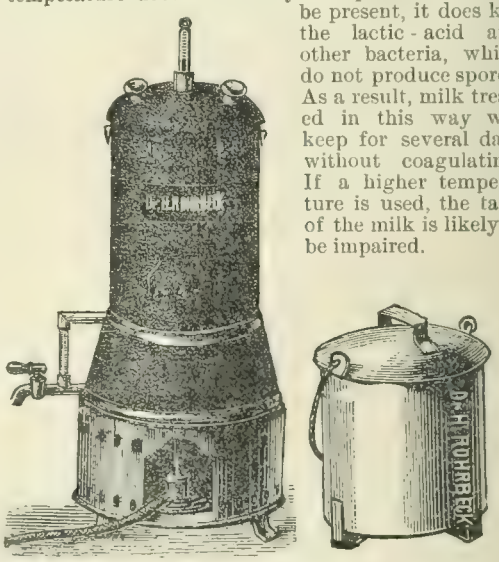


Fig. 5064.—Koch's Steam Sterilizer.

3. *Sterilization in Flowing Steam.*—Several forms of apparatus have been devised for this purpose. Among the earliest is the well-known form which bears Koch's name. This apparatus is used almost entirely in Ger-

many, and to a considerable extent in this country. It is shown in Figs. 5064 and 5065.

It consists of a cylinder of galvanized iron, or better of copper, which can be given such dimensions as may be desired. Ordinarily it is about half a metre high and about 25 cm. in diameter. It is surrounded by a thick covering of felt *M*, to prevent loss of heat by radiation. In the interior of the cylinder at *R*, is placed a grate which serves as a support for the pail and other vessels to be disinfected. The water in the lower compartment is heated by one or more large gas burners. Above it is closed with a cover *D*, which is also covered with felt. A central opening permits the escape of steam, and can be used for the insertion of a thermometer. The pail shown to the right of the sterilizer has a grating for a bottom, to allow free access of the steam, and in it are placed the articles to be sterilized.

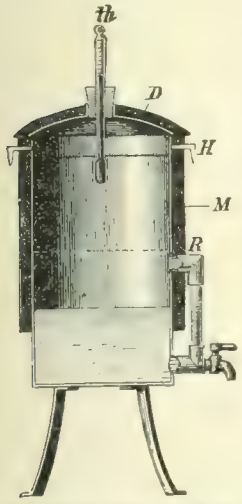
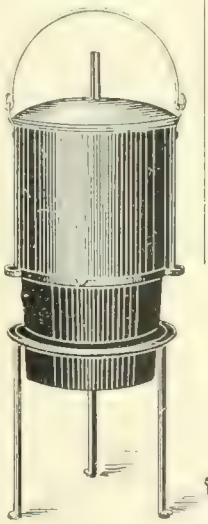


Fig. 5065. Section of Koch's Steam Sterilizer.

The nutrient media are as a rule sterilized by steam. A single heating for one hour in steam at 100° C. is usually sufficient to render the media sterile. Prolonged heating, however, tends to alter the media, and for that reason fractional or discontinuous sterilization is resorted to. The latter has the additional advantage that it renders the medium more surely sterile. There are spores which can withstand steaming for one, and even five or six hours, and if such forms chance to be present, it is evident that the material cannot be sterilized by the single heating for one hour. In the other procedure the media are steamed for fifteen minutes or half an hour, according to the nature of the medium, on each of three consecutive days. The first heat serves to destroy the vegetating germs that may be present. In the interval which elapses between the first and second heating, the spores which are probably present will germinate and are thus converted into the much weaker form, which is then destroyed by the second steaming. The second interval allows any remaining spore, which may have failed to germinate the first day, a chance to do so, and the third heating is expected to dispose of these last organisms. As a rule all media should be incubated for one or two days to make sure that they are perfectly sterile. If any growth develops in the tubes or flasks these should be discarded, and only those which are free should be preserved for use.



Failure to secure sterilization by this procedure is due to one of the following conditions: The temperature which prevails during the twenty-four-hour period which elapses between the consecutive heats may be so high that the spores which are present not only germinate, but the vegetating forms in turn give rise to spores, so that a larger number of resistant forms are present on the second or on the third day than were present in the beginning. Again, it may happen that the temperature is too low, in which case the spores cannot germinate, and hence will be found to resist sterilization. Another source of error, though much less common, was pointed out by Smith. If the spores of anaërobic bacteria are present in a bouillon, they cannot from their very nature germinate under the ordinary conditions, that is, in the presence of the air, and may therefore escape destruction.

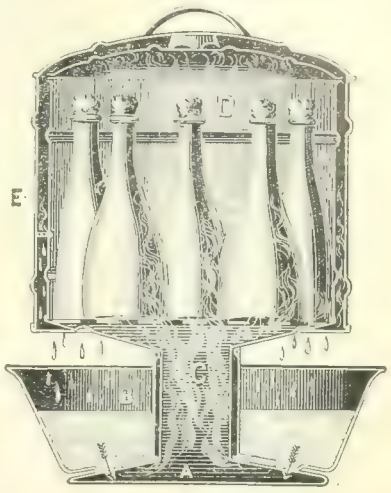


Fig. 5066. Arnold Steam Sterilizer, Sectional View.

In this country, and even in Germany, the Arnold steam sterilizer has met with a very favorable reception. The apparatus is shown in Fig. 5066. It consists of (*a*) a flat, shallow boiler, holding but a small amount of water, and therefore requiring but a minimum amount of heat to produce steam; (*b*) a reservoir placed upon the boiler, which it constantly feeds and insures the constant formation of steam; (*d*) a covered steam chest or receiving vessel, placed above the reservoir and connected with the boiler by a cylindrical tube of large diameter (*c*); and (*e*) a hood, covering the receiver and enclosing an air space, which is constantly supplied with escape steam. The hood and the steam jacket which it encloses prevent variations in temperature in the receiving vessel so long as the heat applied to the boiler remains unchanged.

A cheap and thoroughly efficient steam sterilizer adapted for individual work is shown in Fig. 5067. This consists of an ordinary Hoffmann iron water-bath 10–20 cm. in diameter. On this is placed a copper pail (20 × 20 cm.), which is provided with a perforated bottom. Two perforated rings on the inside allow the passage of steam, and prevent the cotton of the tubes from coming into contact with the side of the steamer. The tubes filled with media are placed in the pail, and this is then set on the water-bath, the water of which has been previously raised to active ebullition. In a few minutes steam will issue from the tube in the top of the cover. It is always advisable to take the temperature of the vapor as it issues from a sterilizer and to count the time of exposure from the moment that the vapor actually shows the temperature of steam, that is 100°.

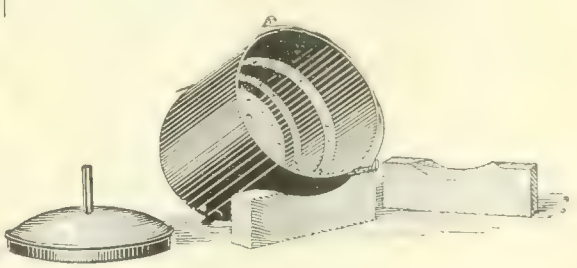


Fig. 5067.—Novy Steam Sterilizer.

4 *Sterilization by Steam Under Pressure.*—This procedure is used almost entirely by the French workers. Its usefulness is such as to merit a wide introduction into this country. The apparatus, which is designated as an

autoclave, is shown in Fig. 5068. It consists of a strong boiler, in the bottom of which a small quantity of water is placed. The articles to be steamed are placed in a wire basket, which is set on the bottom of the boiler. The lid is closed with a rubber gasket and securely held in place by thumb screws. Inasmuch as the amount of aqueous vapor in a given space as well as the temperature, in the case of confined steam, is greater than with flowing steam, it follows that the autoclave is considerably more efficient. Thus steam at 130° C., under pressure, will destroy instantaneously spores which would resist flowing steam at 100° for five or six hours.

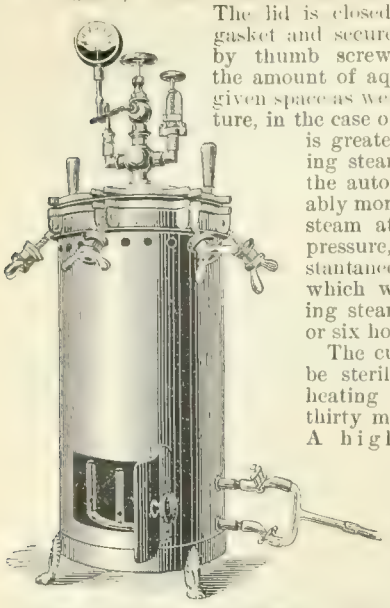


FIG. 5068.—Chamberland Autoclave for Sterilizing by Steam Under Pressure. (Novy.)

The culture media can be sterilized by a single heating for fifteen to thirty minutes at 110° C. A higher temperature should be avoided, as it tends to alter the reaction of the media. Glass apparatus, filters, rubber, etc., can be sterilized by heating at 120° for half an hour. Infected animals can be subjected to 120° for the same length of time, or to 130° or more for a less period.

It must be remembered that the autoclave requires more care than an ordinary sterilizer owing to the danger of explosion. The following points should be observed in its use: Enough water should be present; after the burners are lighted, the steam valve should be left open until all the air has been expelled; when the steam has flowed rapidly for one or two minutes the valve is closed; as soon as the desired temperature is indicated on the gauge, the burners are turned down, so that this temperature is maintained for the required time; the burners are then turned off, but the steam valve is not opened until the temperature has fallen below 100°, after which the lid can be removed. The safety valve should be tested to open at about 125° C. It is a good rule not to leave the autoclave out of sight while the temperature is rising.

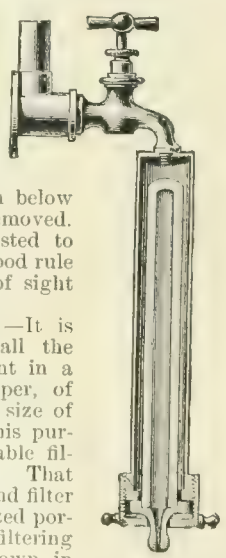


FIG. 5069.—Pasteur-Chamberland Filter.

5. *Sterilization by Filtration.*—It is possible to remove completely all the organisms which may be present in a liquid by filtration. Filter paper, of course, on account of the small size of the bacteria cannot be used for this purpose. There are only two reliable filters for bacteriological work. That known as the Pasteur-Chamberland filter is the best, and is made of unglazed porcelain. The form, as used for filtering water for domestic use, is shown in Fig. 5069. The original French filters are to be preferred to the German imitations. They are made in two grades; that marked *F* is more porous than that marked *B*.

The Kitasato filter, a narrow form of the above, is also made of unglazed porcelain, and is intended for the filtration of very small amounts of liquid. This can, however, be done also with the former. It is shown in Fig. 5070.

The Berkefeld filter (Fig. 5074) consists of closely packed infusorial earth. It can be obtained in several sizes, having the general shape of the Chamberland Pasteur bougie. It is considerably more porous than the porcelain filter, and is therefore adapted for rapid filtration, but it should be borne in mind that it is more likely to allow the passage of bacteria.

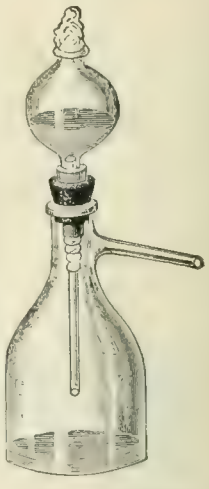


FIG. 5070.—Kitasato's Filter.

A useful form of apparatus for holding the Pasteur-Chamberland bougie, that of Martin, is shown in Fig. 5071. It consists of a metal cylinder with a funnel-shaped top, which permits the filtration of the culture through filter paper previous to its passage through the bougie, and thus obviates or lessens the clogging of the latter. A rubber ring serves to make a tight joint when the bougie is held in place by the lower screw cap. The lower end of the bougie is connected with a piece of vacuum rubber tubing to a globe receiver. The entire apparatus is sterilized by heating in an autoclave. The filtration may be carried on by gravity or an aspirator may be connected with the upper tube of the globe receiver. When the filtrate is to be transferred, the drawn out side tube is scratched near the end with a file, and then broken off, after which the tube is flamed and the liquid is drawn off into sterile tubes or flasks. This globe receiver can be used until the drawn out tube is too short, when a new tube is fused on.

A better form of a globe receiver is shown in Fig. 5074. This is provided with three side tubes, which are plugged with cotton, after which the receiver is sterilized in a dry-heat oven. When it is to be used, the cotton is removed from the tube *D*, which is then connected with the sterile bougie by means of a piece of sterile vacuum tubing. The horizontal tube *F* is similarly connected with the sterile drawn-out glass tube *G*. The tube *E*, with its cotton plug in place, is connected with a Chapman pump. The filtrate may be withdrawn by means of a sterile bulb pipette, or in the same way as from the receiver of Martin. The advantage lies in the short rubber tubing, compactness, and the convenience in attaching the drawn-out tube. This vacuum receiver can be obtained in several sizes, such as one-quarter, one-half, one, and one and one-half litre capacity.

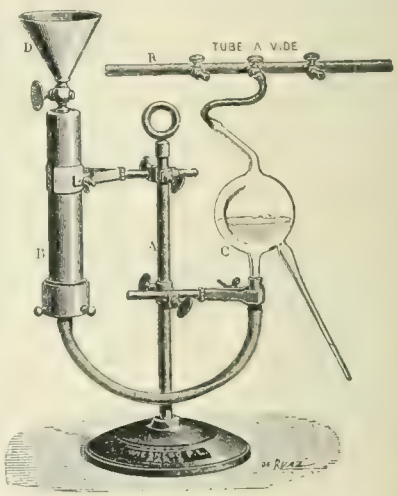


FIG. 5071.—Martin's Filter.

Instead of a metal cylinder to hold the bougie, Novy has devised one of glass. This is shown in Fig. 5072. The necessary tight joint between the bougie and the glass cylinder is made with a rubber ring, and the bougie is brought up tight into place by means of small vises, which act on the flange and on an iron washer. The ar-

rangement is shown in Fig. 5073. If desired the liquid can be filtered under pressure, in which case the rubber stopper at *H* is connected with a tank of compressed air. The cylinders are made to withstand a pressure of over one hundred pounds.

The Berkefeld filter may be attached to the above glass cylinder by means of a rubber and iron washer and the clamps mentioned (Fig. 5074). A more convenient arrangement is to use a cylinder of brass of suitable length and width, threaded at each end. The lower end is provided with a screw cap, through which the metal end of the Berkefeld bougie is passed The upper end is also closed with a screw cap, provided with a three-eighths of an inch nipple,

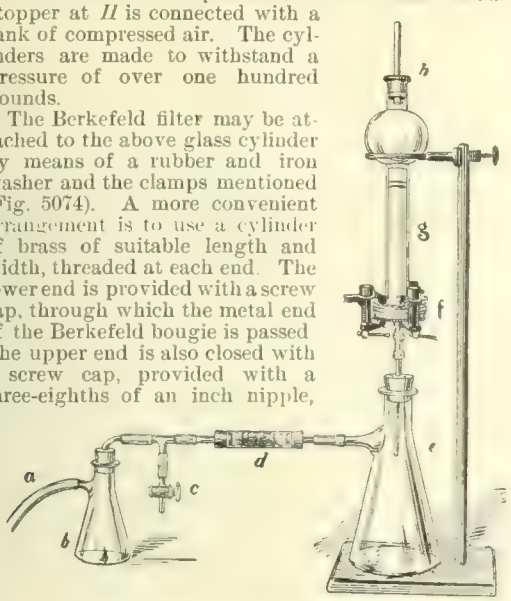


Fig. 5072.—Novy's Filtering Apparatus.

which serves to connect the cylinder with the compressed air The tip of the Berkefeld is connected with a globe receiver. The filtration can then be carried out by gravity, by aspiration, or by pressure.

The filtration of liquids constitutes an exceedingly important part of bacteriological technique. By its means the soluble products of bacteria may be separated from the solid cells. In this way the toxins of many pathogenic bacteria are prepared. Again it is by the filtration process that it has been possible to demonstrate the existence of the so-called ultra-microscopic organisms. While the common bacteria will not pass through a filter, there are a number of diseases in which the cause is so minute that it will go through the Berkefeld, and at times, even through the Pasteur-Chamberland bougie. Yellow fever, sheep pox, foot-and-mouth disease, contagious pleuro-pneumonia of cattle, chicken pest, rinderpest, horse sickness, molluscum contagiosum of birds, and the "mosaic disease of tobacco" are of this class. So also is that of rabies. The fact that a given filtrate infects is not proof that the cause is always in this extremely minute form. It may be that the real organism is relatively large, as in the case of the rat trypanosome, and yet Berkefeld filtered cultures of this will often infect animals. This is due to the existence of a minute stage in the development of the organism. It is therefore to be expected that the pathogenic protozoa, though they themselves may be large, may give rise to filterable sporozoites.

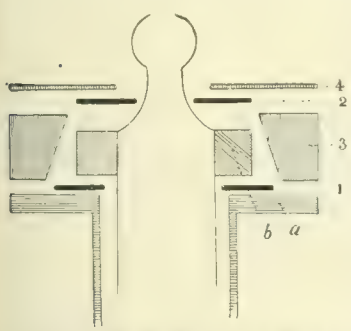


Fig. 5073.—Connections for the Novy Apparatus. 1, 2, 3, Rubber rings; 4, iron washer.

6. *Sterilization by Chemicals.*—This principle is applicable only to a limited extent to nutrient media. The addition of such substances as carbolic acid or mercuric chloride will serve to destroy the organisms which may be present, but since these compounds cannot be removed from the medium, it follows that it cannot be used for culture purposes. A few substances have, however, been used with this object in view. Thus if chloroform is added to milk or blood serum, and is allowed to act long enough, it will bring about sterilization. The remaining chloroform can finally be driven off by means of gentle heat and by aëration. Ether has been used in the same way, and indeed this is a useful procedure for sterilizing such weak cultures as those of cholera. Glycerin, as is well known, is added to vaccine with the object of destroying the common pus-producing organisms which are so often present. It certainly will in time destroy all of these accidental bacteria, but unfortunately prolonged exposure of the vaccine virus to the glycerin damages it as well.

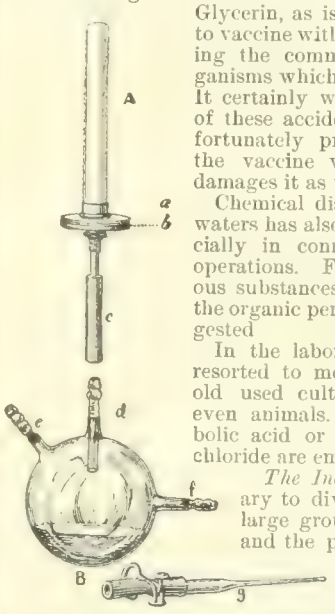


Fig. 5074. Berkefeld Filter showing Manner of Attachment. Globe receiver. Novy.

Chemical disinfection of drinking-waters has also been proposed, especially in connection with military operations. For this purpose various substances, such as bromine and the organic peroxides, have been suggested

In the laboratory this method is resorted to more or less to sterilize old used cultures, test tubes, and even animals. Five-per-cent. carbolic acid or 0.1-per-cent. mercuric chloride are employed.

The Incubator.—It is customary to divide bacteria into two large groups — the saprophytic and the parasitic—according as to whether they grow in nature on dead matter or in the living body. Among the latter are classed the disease-producing bacteria. In general the optimum temperature for the growth of the saprophytic organisms is about 25° C., whereas the pathogenic bacteria thrive best at the temperature of the body. In order to supply this requirement it is necessary to use an incubator or thermostat, the temperature of which can be maintained without variation at any desired level. Various forms of apparatus have been devised for this purpose; that of Koch is shown in Fig. 5075. It consists of a double-walled box of copper, the sides and top

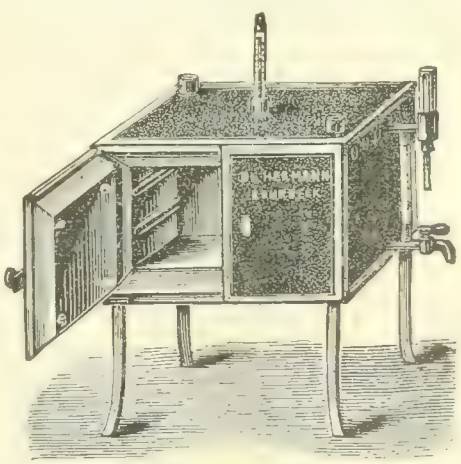


Fig. 5075.—Koch's Incubator.

being covered with felt. The space between the walls is filled with water. In the top is an opening communicating with the interior air space, and in it a thermometer is placed to indicate the temperature. The openings in the corners communicate with the water space. One of these is intended to hold the thermo-regulator, while

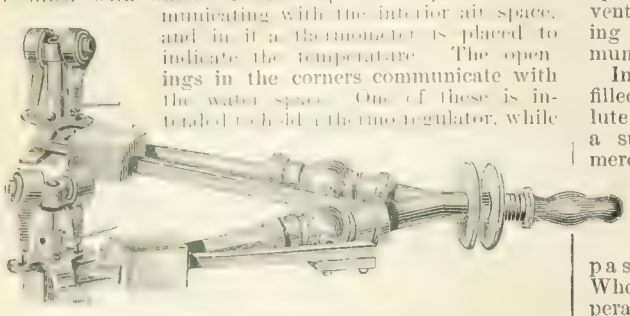


Fig. 5076. Koch's Safety Burners.

the other serves for the addition of water. Inner and outer doors are provided, and in the better models provision is made for ventilation and for keeping the air moist.

The apparatus may be heated with an Argand burner. The ordinary Bunsen burner is not used because of the danger of "shooting back." The Koch safety burner is to be preferred, for it automatically shuts off the supply in case the gas should by any chance happen to be turned off. It consists of two iron spirals which, as they are heated, expand, and in so doing communicate this motion to an arm which then swings under and supports the weighted lever of the valve. If by any accident the flame should become extinguished, the spirals cool and contract; this causes the supporting arm to swing out from under the lever, which then falls and thus shuts off the gas (see Fig. 5076).

In case gas is not available the incubator is heated with an oil lamp. The Sartorius model is especially well constructed for this form of heating. A good substitute can always be found in the ordinary egg incubator. In a few places the heat is supplied by means of electric hot plates.

By far the most important accessory to an incubator is a thermo-regulator, which will automatically control the supply of gas and hence the temperature of the oven. Several of the more common forms are shown in Fig. 5077. The Reichert form, though very widely used, is far from being the most satisfactory. The lower bulb is filled with mercury, which as the temperature rises shuts off the opening through which the gas enters. In order to prevent the flame from being extinguished a minute opening is made in the gas delivery tube whereby a minimum flame can be maintained.

In the Bunsen form the lower compartment is nearly filled with a mixture of equal parts of ether and absolute alcohol, after which a sufficient quantity of mercury is added to act as a valve. The upper part is closed with a stopper, through which passes the gas tube. When the proper temperature is reached, this tube is pushed down till the gas flame drops. The minimum opening prevents total extinguishment. By careful manipulation the regulator can be set at any temperature which may be desired.

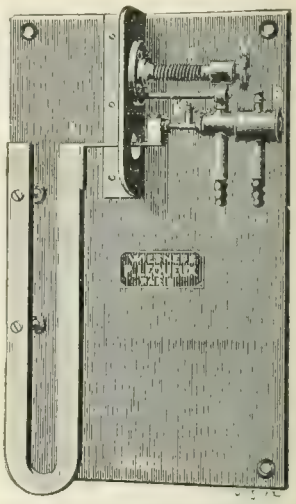
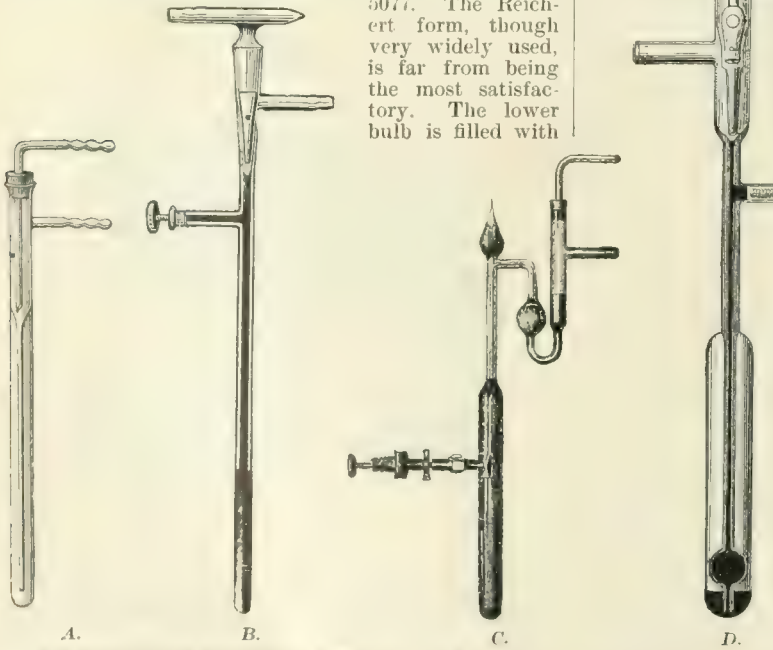


Fig. 5078. Roux Metallic Thermo-Regulator.

In both the Novy and Dunham forms the lower bulb is filled with absolute alcohol. As this expands it acts against a column of mercury, which in turn shuts off the supply of gas. The lateral screw permits the adjustment of the regulator to the desired temperature. In the former the minimum supply can be regulated to a nicety. This enables it to be used for a water-bath, or for a small or large incubator. It can be obtained with the alcohol cylinder of different sizes, according to the use for which the apparatus is intended.

The metallic regulator of Roux is intended for controlling the temperature of large water-baths and of incubator rooms, for which purpose no better device can be found. It is made in the two forms, the straight and the U shape, shown in Fig. 5078. It consists of two metal bands having different coefficients of expansion. These are soldered together the full length. As the temperature rises, the free upper arm moves from and thus releases a spring valve, which shuts off the main supply of gas. A minute opening serves to supply a minimum amount of gas, and thus prevents extinguishment of the flame.

The incubator described in its several modifications answers all ordinary purposes. In large laboratories they can, however, be dispensed with almost entirely, and their place is taken by the incubator room. By this is meant a room, usually about eight feet cube, which is maintained at a constant temperature. This arrangement



A. B. C. D.

Fig. 5077. Thermo-Regulators. A, Bunsen's; B, Reichert's; C, Dunham's; D, Novy's.

was first employed at the Pasteur Institute, where the heat is conveyed to the room by means of large pipes along the wall, filled with water, or better with glycerin. The circulating liquid is heated by a small gas stove placed on the outside of the room.

A more simple and thoroughly efficient procedure is to place a small gas stove in the centre of the room. This stove, which can be obtained of the French dealers, is so constructed that the gases of combustion are carried out of the room into a flue.

Another procedure of limited application is to heat the room with steam coils. The regulation of the heat in this case is accomplished by means of an automatic steam valve operated by compressed air.

The construction of the room requires no special care. The walls, whether of brick or of plaster, should be given several coats of white zinc. Shelves, water, gas and electric light, and a window should be provided.

The regulation of the temperature in the rooms heated by gas is done by means of the Roux **U**-shaped regulator. All the connections should be of metal to lessen the chances of fire. In order to have a temperature record it is advisable to place in the room a thermometrograph, the best form of which is made by the Richard Frères, of Paris.

Gas-Pressure Regulator.—The best results with any form of thermo-regulator are obtained when the gas pressure is constant, or nearly so. When the variation is considerable it is advisable to pass the gas through a pressure regulator before it reaches the thermo-regulator. There are several forms of apparatus for this purpose. The Moitessier regulator is shown in Fig. 5079. It consists of a cylinder *A*, which is filled to the level of *G*, with a mixture of equal parts of glycerin and water. On this is floated the metal shell *B*. The gas is admitted to the interior of *B*, through the tube *K*, the pressure being indicated by the manometer *P*. The gas flows into *B* until it is filled, when it raises it up and shuts off the supply of gas by closing the valve *D*. The pressure on the burner is regulated by the weights placed in the pan *H*, which is connected with *B* by the rod *G*. The amount of pressure on the burner is indicated by the manometer on the left of the apparatus. The burner is connected with the apparatus by means of a rubber tube attached to *I*, and the height of the flame is regulated by the stopcock *M*.

A cheaper and more simple regulator is that devised in Novy's laboratory by Murrill and shown in Fig. 5080. The gas passes into a cylinder which floats in liquid petroleum and leaves by two tubes at the bottom, one of which is connected with the thermo-regulator, the other with a manometer. The cylinder is weighted so as to give the desired pressure to the outflowing gas.

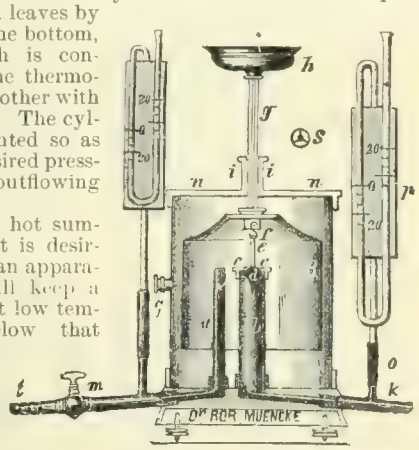


Fig. 5079. Moitessier's Gas-Pressure Regulator.

During the hot summer months it is desirable to have an apparatus which will keep a fairly constant low temperature, below that which would cause the gelatin cultures to melt. There are incubators constructed for this purpose which furnish a supply of ice-cold water when the temperature rises above a given point. If the temperature drops too low an electric lamp is turned on.

When the temperature of the water as it leaves the ground is about 15° it is possible to use the simple apparatus shown in Fig. 5081. This is made of galvanized iron. The inner box is held in place by means of a couple of stout rods. The water enters at the bottom through the small tube, which stops short on the inside of the outer box. The water then flows under and around the inner box, and eventually reaches at the farther end the wide outflow tube. The end of this is turned up and is provided with a short piece of rubber tubing. By moving this up or down the level of the water in the box can be regulated. By regulating the flow of the water it is possible to maintain a fairly constant temperature in the inner compartment.

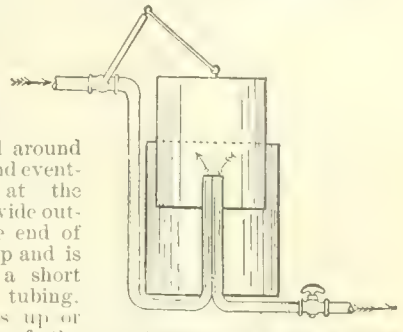


Fig. 5080. Murrill's Gas Pressure Regulator. Cross-section. (Novy.)

The Methods of Cultivation.—The fundamental basis of bacteriology may be said to be the fact that it is possible to cultivate artificially, and that in pure condition, nearly all of the known forms of bacteria. Until methods had been devised for this purpose it was not possible to determine definitely the part played by any organism either in the ordinary phenomena of fermentation or in the more mysterious processes of disease. To arrive at a demonstration of the causal relation of a given organism to the change which it is supposed to induce it is necessary to do two things: First, the organism must be isolated in pure culture; and second, the pure culture, once obtained, must be maintained by transplantation. The pure culture thus kept up through a series of transplantations, or generations as they are called, can then be tested upon animals to see if it will reproduce the disease; upon suitable media to ascertain if it will cause the kind of fermentation, the pigment, or the light which it is supposed to produce.

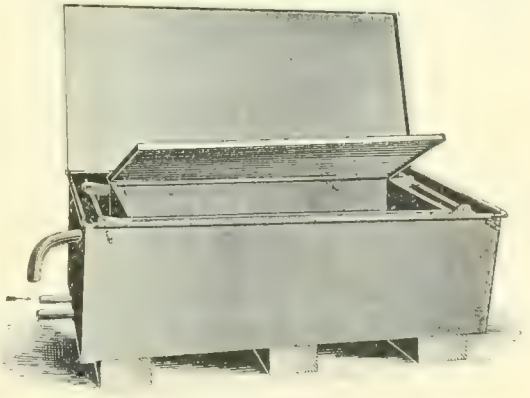


Fig. 5081. Novy's Low-Temperature Incubator.

By a pure culture is meant one which is derived from a single cell. A given bacterium, small as it is, multiplies by division, and thus gives rise to two new individuals. These in turn grow and divide, yielding four cells. This process is kept up till many millions of organisms constitute the offspring of a single cell. Inasmuch as the division of bacteria is very rapid under favorable conditions, many dividing every half-hour, it follows that in a few hours a visible growth may be seen where at the beginning but a single cell was present. If the medium in which they are growing is liquid, it will usually become cloudy because of the disseminated bacteria.

The early methods of cultivation as employed by Pasteur made use of liquid media. Under these conditions it was exceedingly difficult to obtain pure cultures, and indeed it was largely a matter of chance and patience. Suppose that a given liquid contains two kinds of bacteria; in order to separate these so as to have a single cell as a starter for the pure culture it would be necessary so to dilute the liquid that in all probability a drop, or a cubic centimetre, would contain but one cell. This small quantity would then be taken and transferred to a sterile medium, and in this way it would be possible to obtain presumably pure cultures. Failure, however, was necessarily frequent and the element of doubt always remained.

The introduction of the nutrient gelatin by Koch made it possible to secure pure cultures with the greatest of ease. All that was necessary was to inoculate the liquefied gelatin with the mixture of bacteria, and after thorough agitation so as to separate each cell from its neighbor, to pour the liquid on to the surface of a sterile plate. The gelatin now solidifies and imprisons, as it were, the separated cells. Each of these now multiplies and reproduces its kind; eventually, in the course of a day or two, a small growth, perhaps of the size of a small pinhead, appears. This is called a colony, and since it is derived from a single cell it constitutes a pure culture. Such is the principle of the dilution method for obtaining pure cultures. The isolation once accomplished, all that is necessary is to transplant the colony to sterile culture media so as to keep up the growth.

The transferring of bacteria is usually done by means of a platinum wire. The wire, which should be about two inches long and fairly stiff, about No. 21 in size, is fused into the end of a glass rod. According to the object in view it is either straight, bent, or is provided with a loop as shown in Fig. 5082.

Fig. 5082. Platinum Wires, Fused in Glass Rods.

At times a bunch of very fine platinum wires attached to a holder, the so-called Kruse's brush, is used to spread the material over the surface of the media. A glass rod bent at right angles is also very useful for this purpose. The Roux spatula of nickeled steel was first employed for the purpose of transplanting bits of diphtheritic membrane to the culture tube. A similar spatula made of thick iron wire is extremely useful for transferring moulds and compact growths, such as that of actinomyces. The Nuttall platinum spear is particularly useful for transferring bits of tissue, blood, etc., to the nutrient media. These two instruments are shown in Fig. 5083.

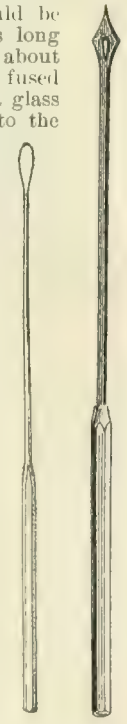


Fig. 5083.—*a*, Roux spatula; *b*, Nuttall's platinum spear.

The transferring of liquids, in large or in small quantities, can best be done by means of drawn-out glass tube pipettes, as is practised by the Pasteur School. This technique is at once simple and invaluable. The preparation of these pipettes will be understood from Fig. 5084.

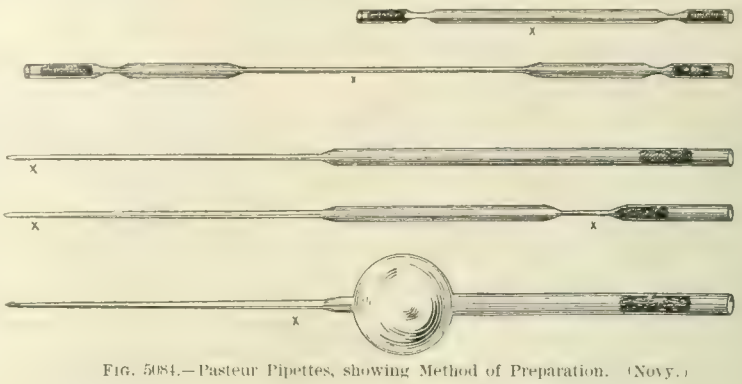


Fig. 5084.—Pasteur Pipettes, showing Method of Preparation. (Novy.)

The glass tubing, which has a diameter of about 8 mm., is cut up into lengths of about twelve inches. By means of the blast lamp a slight constriction is made at about two inches from each end. This serves to prevent the cotton plug from falling down, and also tends to keep the liquid from reaching the cotton. The ends of each tube are then carefully rounded out in the flame. A piece of cotton is then pushed into the end of each tube. The tubes thus prepared (Fig. 5084, *a*) are then sterilized in the dry-heat oven, after which they may be stowed away for future use.

Whenever it is desired to make a pipette, one of these tubes is heated in the middle in a blast flame, and when the glass has thoroughly softened, the two halves are slowly drawn apart. A relatively wide, thick-walled capillary, about sixteen inches long, is thus obtained (Fig. 5084, *b*). This is then sealed in the flame in the middle, and the result are two pipettes. For transferring larger quantities of liquid a bulb is blown in the pipette (Fig. 5084, *e*). This is made by directing a narrow blast flame against the tube, which is at the same time rotated. As the glass softens the ends are slightly pushed together, so as to form a thick ring of glass. This is repeated once or twice. Finally a large blast flame is turned on, and when the thickened glass is perfectly soft, the end is brought into the mouth and the bulb is blown. The glass should be rotated during this operation, and in fact in all work of this kind.

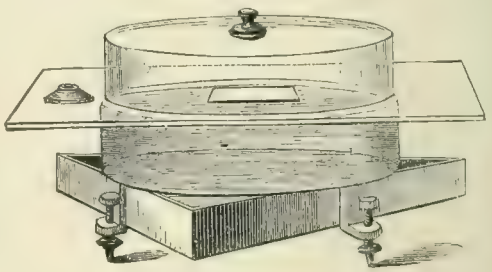


Fig. 5085.—Koch's Levelling Apparatus.

To use a pipette, the mouth end should first be rolled for a few seconds in a flame so as to insure sterility; the capillary end is then scratched with a file and the tip is broken off, after which the capillary is flamed. As soon as the tube has cooled, which fact can be ascertained by

blowing through the pipette against the back of the hand, it is ready for use. The closure of the pipette when it is filled with the liquid is effected by means of the tongue.

The great value of the pipette lies in the fact that it can be made in a few minutes, and can be used to transfer liquids from one tube to another, for drawing blood from the heart, fluids from the cavities, etc. It is indeed even more useful than a platinum wire.

Plate Cultures.—Solid media, such as gelatin or agar, either plain or modified, are employed for this purpose. The starting-point in this method were the slide cultures used by Koch in his early investigations. The liquefied gelatin was poured upon the surface of sterile glass slides, which were levelled and kept cool by means of the apparatus shown in Fig. 5085. The lower dish was filled with ice water and the whole was set true by the aid of a small spirit level. A series of parallel streaks was then made on the solid gelatin by means of a platinum wire, which was dipped in the material to be planted. A number of slides were thus made, after which they were stacked on glass benches (Fig. 5086), and placed in a moist chamber to develop (Fig. 5087). The first streak, on account of the large number of organisms planted, would probably yield a continuous solid growth. The next streak would have fewer germs, and the succeeding ones still less until eventually only single germs would be deposited, separated by an appreciable distance from the following ones. Wherever a single organism was deposited, as a result of multiplication, a colony would soon make its appearance. (See Plate LXI.)

The slide method was soon improved by substituting larger glass plates (10 × 13 cm.). Instead of making

Fig. 5086.—Glass Benches and Culture Slides.

streak dilutions as just given, the gelatin was liquefied, inoculated, and poured out upon the sterile plates, which were cooled on the plating apparatus. This method of plating may be used when the special Petri dishes, ordinarily employed, are not obtainable. The fact that the method required a lot of apparatus, slides, slide-box, levelling apparatus, ice, moist chamber, etc., as well as the fact that contamination from the air and from the dripping of the superposed plates was unavoidable, led Petri to introduce the modification which has almost entirely supplanted the older method.

Gelatin Petri Plates.—In this method, as in the preceding, the gelatin is first melted by immersion in warm water for a few minutes. By means of a sterile, looped, platinum wire a small quantity of the material to be examined is transferred to a tube of liquefied gelatin, marked 1. By means of the wire the material is thoroughly mixed with the gelatin. Another tube, marked 2, is then placed beside the first, from which three loopsful of gelatin are carried over to tube 2, with the contents of which they are well mixed (Fig. 5088). A

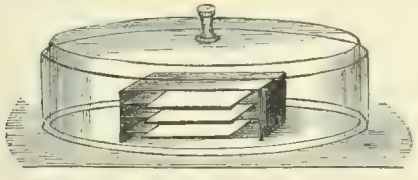


Fig. 5087.—Moist Chamber with Stacked Plates.

third tube, marked 3, is then placed beside number 2, and three loopsful of gelatin are transferred from tube 2 to tube 3. It is evident from this procedure that even if the first tube received a million germs the second tube would contain only a small fraction, and the third tube would contain still less. The platinum wire must of course be sterilized whenever an inoculation is made into a new tube.

A number of Petri dishes (Fig. 5089), which are 10 cm. in diameter and 1 cm. high, are previously sterilized by heating in a dry-heat oven for one hour at 150°, or for a few minutes at 200°, and allowed to cool. To pour the plate, the cotton is removed from one of the tubes, and the open end is rolled for a few seconds in the flame so as to sterilize it. In a few seconds the end of the tube becomes cool, after which the contents are poured out into the Petri dish. The lid of the latter is removed just sufficiently to allow the gelatin to be introduced. By tilting the gelatin is then spread all over the bottom of the dish. The latter is then set aside in a cool place for the gelatin to set. With a good gelatin this will take place even in the ordinary room within a few minutes. The remaining gelatin tubes are poured in the same manner. Each plate should be numbered to correspond to the tube from which it was made. They should be marked also with the date and the kind of material used. A Faber's colored wax pencil is used for this purpose.

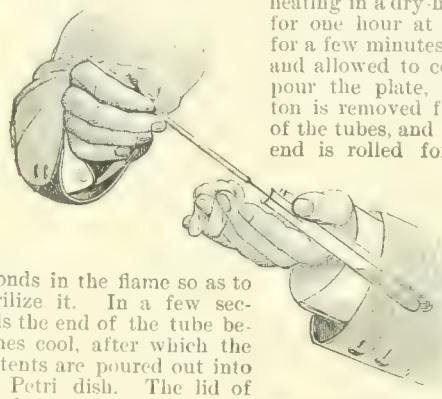


Fig. 5088.—Method of Holding the Tubes when Making Dilutions.

Agar Petri Plates.—Inasmuch as gelatin melts at about 25° C. it follows that the method just given cannot be used when the organism requires the temperature of the incubator. In such cases it is necessary to resort to the use of agar. The nutrient again is first melted by heating in a water-bath at 100° C. The flame is then turned out and the tubes are allowed to cool in the water bath until a temperature of about 45° is reached. The agar solidifies at about 40°, and consequently the dilution must be made rapidly and the plates poured before the

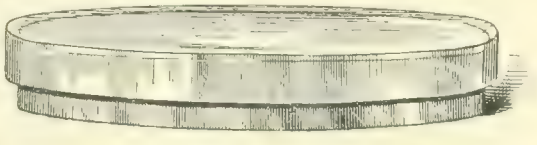


Fig. 5089.—Petri Dish for Plating.

point is reached. Dilution cultures are made in the same way as just given for gelatin. The three agar tubes are then poured out into the corresponding sterile Petri dishes. The agar promptly solidifies, and for that reason the spreading of the agar over the bottom must be hastened. The agar plates are then set aside to develop either at the temperature of the room or at that of the incubator.

Esmarch Roll-Tube Culture.—This modification of the plate method does away with the use of any special container other than the test tube. The dilutions in gelatin are made in the usual way. According to the original directions the cotton plug was cut off short, and the end of the tube was covered with a close-fitting rubber cap. The tube was then immersed and rotated in an almost horizontal position in ice water. The gelatin solidified in an even film over the inside of the test tube (Fig. 5090).

A more convenient way of rolling the tubes was de-

vised by Booker. With the aid of a large test tube filled with warm water a groove is melted into a block of ice. The gelatin tubes are then rolled in this groove until the gelatin solidifies in a smooth, even film. Nuttall has modified this procedure by replacing the ice block with a marble block provided with grooves for the test tubes. Running tap water serves to cool the tubes.

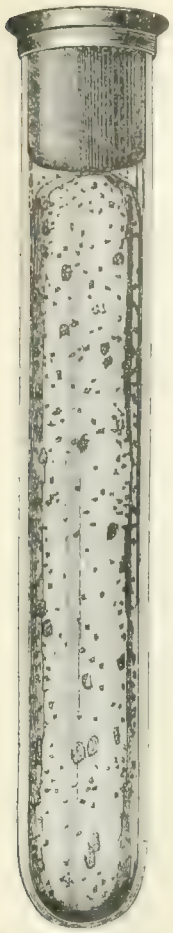


FIG. 5080.—Esmarch's Roll Culture.

If the tubes are not rolled smoothly they can be softened by gentle warming and rerolled. One advantage of this method lies in the fact that desiccation can be retarded more than with the other methods. Air contamination is likewise diminished. On the other hand, the presence of a few liquefying bacteria may spoil the tube. The Esmarch roll tubes should be kept in a cool place to prevent melting. When the colonies develop they may be examined by placing the tube on the stage of the microscope. To transplant the colonies a platinum wire, provided with a hook, as shown in Fig. 5082, should be used.

Shake Cultures. — Dilutions are made in gelatin or agar as heretofore described. The tubes are then solidified in an upright position and allowed to develop. If it is desired to transplant a given colony the test tube should be scratched with a diamond at about the level of the colony. On touching the scratch with a hot rod, the crack can be led around the tube, after which the two parts can be separated. By means of a sterile knife the medium can be cut and the colony exposed. In the case of agar the entire cylinder of agar can be forced out of the tube into a sterile dish by the cautious application of a flame to the lower end of the tube.

The method offers a convenient means of determining whether or not the organism planted generates gas. If such is the case gas bubbles will make their appearance in the medium. As will be seen later this method is also useful in connection with the cultivation of anaerobic bacteria.

Streak Cultures.—This procedure, which is essentially the same as that used by Koch in his slide cultures, is very frequently made use of at the present time. Thus, sterile gelatin or agar may be poured into sterile Petri dishes, and after the material has solidified a series of parallel streaks may be made with an infected wire. The Kruse platinum brush may be used to spread the organisms over the surface. A narrow glass rod, bent and flattened at the end, has been used for spreading gonorrhœal pus over plates. Cotton swabs are used for the same purpose in the case of diphtheria.

As in the case of the Esmarch roll tube, the Petri dish may be omitted in this method. In that event the gelatin or agar is melted and allowed to solidify in an inclined position. The streaks are then made on the surface of the inclined medium. Potato tubes are inoculated in the same way. (See Plates LX. and LXI.)

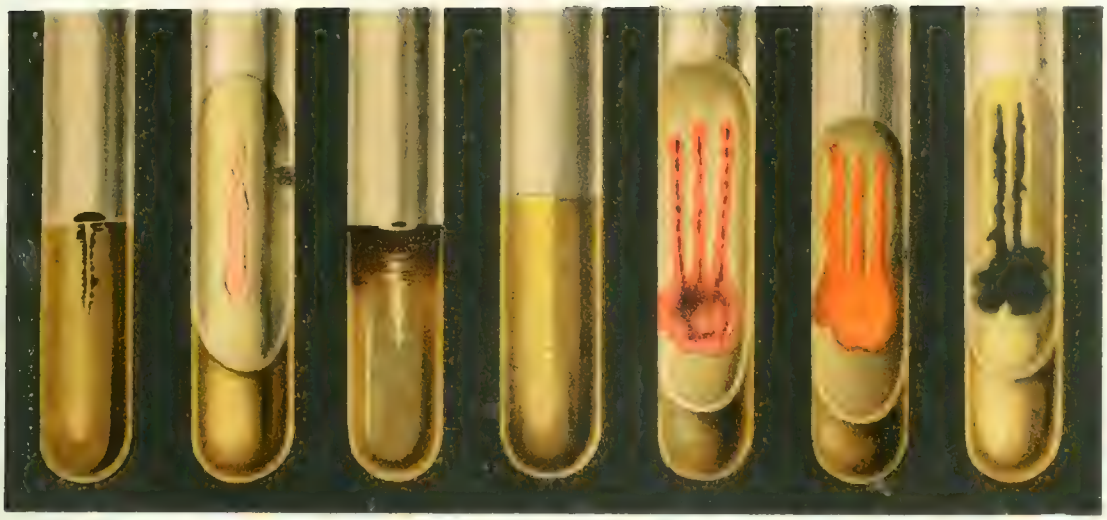
To obtain perfectly isolated colonies by this method the same wire should be used to make parallel streaks on each of four or five tubes. When the colonies develop transplantations can be made by means of a bent wire.

Hanging-drop Cultures.—A concave or well slide, shown in Figs. 5105 and 5106, is used. The cover glass must first be sterilized by passing it several times through a flame. A large drop of sterile bouillon is then placed in the centre, and this is then inoculated with the germ to be studied. The slide with a ring of vaseline is then inverted and brought down upon the cover-glass, after which the preparation is turned over. Care must be taken to see that the vaseline closure is perfect. This method of cultivation is used to study the multiplication of the bacteria under the microscope.

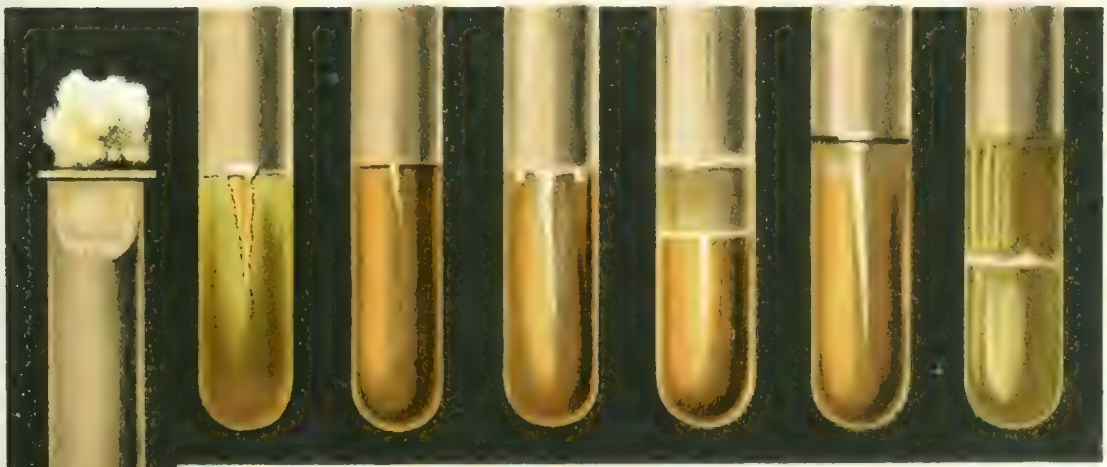
Hanging-block Cultures.—In order to be able to study the morphology and the multiplication of the diphtheria bacillus to better advantage than that afforded by the hanging drop, Hill devised the following procedure: Melted nutrient agar is poured into a Petri dish to a depth of about one-eighth to one-quarter inch. When cool, a block of agar is cut out, about one-quarter to one-third inch square, and of the thickness of the agar layer in the dish. The block is placed, under surface down, on a slide and protected from dust. A suspension of the growth to be examined is then made in sterile water or a bouillon culture is used. The suspension is spread over the upper surface of the block as if making an ordinary cover-slip preparation. The slide and block are then set aside in the incubator at 37° for five or ten minutes, to dry slightly. A clean sterile cover slip is then placed on the inoculated surface of the block in close contact, avoiding large air bubbles. The slide is then removed from the under surface of the block, and the cover slip is inverted so that the agar block is uppermost. With the aid of a platinum wire a drop or two of melted agar is run along each side of the agar block, to fill the angles between the sides of the block and the cover slip. This seal hardens at once and prevents slipping of the block. The preparation is again placed in the incubator for five or ten minutes to dry the agar seal. Finally the preparation is inverted over a moist chamber or suitable well slide. The cover slip is sealed in place with white wax or paraffin. Vaseline cannot be used because it softens at 37°. The "hanging block," thus prepared, is examined on a warm stage or in the incubator room.

Transplantation of Colonies.—The entire object of making plate culture by any one of the several methods given is to obtain single isolated colonies, which can be transplanted to other media and the organism present can then be studied in perfectly pure condition. The colony as indicated is presumably derived from a single cell, and consequently is a pure culture. The transplantations or sub-cultures can be made to gelatin, agar, serum, bouillon, milk, etc. When the colonies are on a plate or in a Petri dish a straight wire is used. The plate is first carefully examined under the microscope, and a colony is selected which is clearly single. If possible it should be the only one in the field of the No. 3, or one-third inch objective. The farther apart that the colonies are the less likely are they to intermingle. As originally directed, the colonies were touched under the microscope by a sterile platinum wire, and in this way a few of the bacteria were removed. Care had to be taken that the wire did not touch the objective or any other part of the gelatin. This operation of "fishing," as it was called, obviously required considerable practice and care. An equally good procedure is to pick out the desired colony under the microscope. The tube of the microscope is then raised, and the point of the sterile wire is brought down so that it cuts the colony and nothing else. The tube is then again lowered and the site of the colony examined to make sure that nothing but the one colony was touched. If such is the case the wire is then used for the sub-culture.

Stab Cultures.—A tube of solid gelatin is taken, the cotton plug is seized by the right little finger and removed. The mouth of the tube is then flamed, after which the wire, laden with the bacteria, is inserted and carefully passed down the centre of the gelatin. The organisms are thus planted along the line of inoculation. The cotton plug is replaced and the tube is labelled and set aside. The form of the growth is then noted from day to day, also the presence of gas, liquefaction, pig-



1. Black Yeast. 2. Red Yeast. 3. Brown Yeast. 4. Yellow Sarcina. 5. Bacillus Prodigiosus. 6. Bacillus Indicus. 7. Bacillus Violaceus.



8. Bacillus Fluorescens. 9. Micrococcus Lactis. 10. Bacillus of Sour Milk. 11. Bacillus Butyricus. 12. Bacillus of Blue Milk. 13. Bacillus of Green Pus.

14. Micrococcus Tetragenus. 15. Staphylococcus of Osteo-myelitis. 16. The same in gelatine. 17. Staphylococcus pyogenes albus. 18. Streptococcus pyogenes. 19. Streptococcus of erysipelas. 20. Streptococcus of Puerperal Fever.

TEST-TUBE CULTURES.

Reproduced from Huber & Becker's "Untersuchungs-Methoden."

ment, etc. The characteristics of the stab cultures are of the very greatest importance in the identification of bacteria. If the gelatin is old and partially dried the passage of the needle is likely to cause a split in the medium. This can be avoided by melting and resolidifying the gelatin. (See Plates LX. and LXI.)

Streak Cultures.—These are also known as "smear cultures." The gelatin or agar tubes are melted and solidified in an inclined position. Similarly solidified blood serum is also used; so also are the potato tubes. The infected platinum wire is drawn along the middle of the surface of the medium by making one single streak. The growth develops along the line of inoculation, and spreads in a more or less characteristic manner. (See Plates LX. and LXI.)

Liquid Cultures.—The tubes of sterile bouillon, milk, serum, etc., are inoculated by simply introducing some of the material from a colony by means of the sterile wire.

The sub-cultures from tube to tube are made in the same way as just given. The drawn-out glass tube pipettes and spatulas can be used to transfer the material from one tube to another, or to flasks.

Anaërobic Cultivation of Bacteria.—The methods just given are essentially aërobic, since there is free access of air. As is well known there are two classes of bacteria with reference to their oxygen requirements. The aërobic bacteria live in the presence of air, while the anaërobic thrive only in the absence of oxygen. In order to cultivate the latter special methods must, therefore, be employed which will supply the needed conditions. Numerous procedures have been devised for this purpose, and to give all of these would be beyond the scope of this article. It will be sufficient to indicate the principles which serve as a basis for these methods, and to describe those which are most widely used.

Fig. 5091.—Liborius Deep Stab Culture, showing Growth of the Tetanus Bacillus.

1. *Exclusion of Oxygen.* This was accomplished by Pasteur in his early work by pouring a layer of oil upon the culture fluid. This served to exclude the air and allowed the bacteria to develop. Koch obtained anaërobic conditions by covering the surface of the gelatin plates with a thin sheet of mica. Others have done the same with glass plates.

The Liborius method of cultivation in deep layers falls under this head. It is simple and is constantly used. Ordinary stab cultures are made in the suitable media, preferably glucose agar. Another tube of agar is liquefied, cooled to about 50°, and the contents of this are then poured on top of the stab culture. Care must be taken to flame the mouths of both tubes so as to avoid contamination. The upper layer of agar serves to keep out the air. The cultures can be prepared equally well by employing agar or gelatin tubes filled with the medium to a depth of about two inches. After the stab is made the line of puncture closes up itself, and the growth then develops in the lower part of the tube, as shown in Fig. 5091.

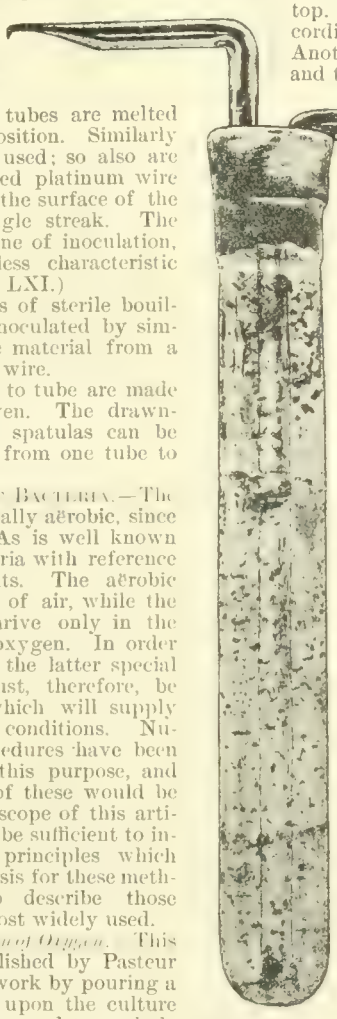


Fig. 5092. Fraenkel's Modification of Liborius Tube for Anaërobes.

Isolated colonies can also be obtained by this method. The liquefied medium is inoculated and dilutions are made as for shake cultures. The tubes are then solidified, and if necessary an additional layer of medium is poured on top. When the colonies develop they can be reached according to the directions given under shake cultures. Another procedure was to make Esmarch roll tubes and then fill the inside with gelatin or agar.

The drawn out glass tube pipettes (Fig. 5084) have been used by Roux for this same purpose. The liquefied medium is inoculated and drawn up into the pipette, which is then sealed above and below the contents. The colonies which develop can be reached by cutting the glass. A somewhat similar procedure was devised by Wright. A short glass tube with constricted ends is used. Each end has a piece of rubber tubing attached. One of these is connected with a glass tube, which projects through the cotton plug of the test tube. The test tube contains bouillon, and this contrivance is sterilized and inoculated. The bouillon is then drawn up into the constricted tube, which is sealed by simply pushing down on the tube, so that both rubber ends are bent back on themselves.

2. *Displacement of Air.*—This is accomplished by passing through the tube or a suitable container an inert gas till all the air has been displaced. Hydrogen is the least injurious gas for this purpose. It can be generated from zinc and sulphuric acid in a Kipp's generator. The gas should be washed by passing successively through alkaline lead acetate, six per cent. potassium permanganate, and finally through a solution of silver nitrate. After passing through the apparatus the gas is sent through a small wash bottle, which serves as a valve to prevent air from entering when the current slows up. Such a wash bottle is shown in Fig. 5093. After the gas has passed for an hour or more it should be tested by applying a light as it leaves the wash bottle. If the flame burns with explosions it is evident that all the air has not been displaced. The operation is continued until the gas burns evenly at the mouth of the tube. Owing to the danger of explosion the light should never be applied to the outflowing gas without the safeguard of the water valve.

One of the earliest attempts at making tube cultures by this method was that of Liborius. He made use of a special test tube with a delivery tube fused into the side. After inoculation of the liquid medium gas was passed through, and finally the neck of the test tube, as well as the end of the delivery tube, were sealed in the flame. This method is of only very limited application, and requires much time and is expensive. Fraenkel's modification is a distinct improvement. Ordinary large test tubes are used. These are provided with rubber stoppers and delivery tubes, as shown in Fig. 5092. After the inoculation of the medium and expulsion of the air, the tubes are sealed in the flame. If it is desired to obtain colonies, the tube can be converted into an Esmarch roll tube, as shown in Fig. 5092.

This principle has been adapted in various ways for the purpose of obtaining plate cultures. Kitasato employed a flat bottle, having a tube fused at the lower end. The dilutions were made in the ordinary tubes, after which the material was poured into these flasks, which were connected in series and hydrogen passed through. Finally the ends were sealed by fusing in the flame, while the neck of each flask was closed with a clamped rubber tube. Several modifications of this bottle have been made, but they are little used, since methods

were soon perfected whereby it was possible to make Petri plates in hydrogen.

One of the earliest attempts in this direction was that of Blücher, who made use of a funnel which was weighted with lead and inverted over the plates in a larger dish. Air was excluded by means of glycerin water. Hesse inverted a glass vessel in a circular trough filled with mercury. Liborius used a copper bell jar which was compressed against a rubber gasket by means of set screws; others made use of bell jars inverted upon a ground glass surface. In many respects the Botkin apparatus is useful. It is shown in Fig. 5093. It consists of a metal rack on which are placed the Petri dishes. This is set in a large outer dish which contains about an inch of liquid petroleum. A bell jar is inverted over the stand. The inflow and outflow tubes are of rubber stiffened by a copper wire on the inside. After the hydrogen has been passed for a sufficient length of time, the tubes are withdrawn and the apparatus is then set aside.

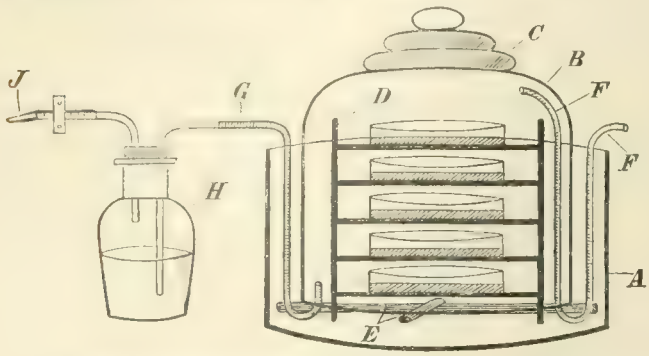


Fig. 5093. Botkin's Apparatus for Plate Culture of Anaerobes.

The Novy apparatus shown in Fig. 5094 leaves little to be desired. The hollow stopper has two perforations, one of which is connected with a glass tube which extends almost to the bottom of the bottle. In the case of the plate apparatus the tube may be continued by means of a piece of rubber tubing. A perfect seal is obtained by simply turning the stopper through an angle of 90°.

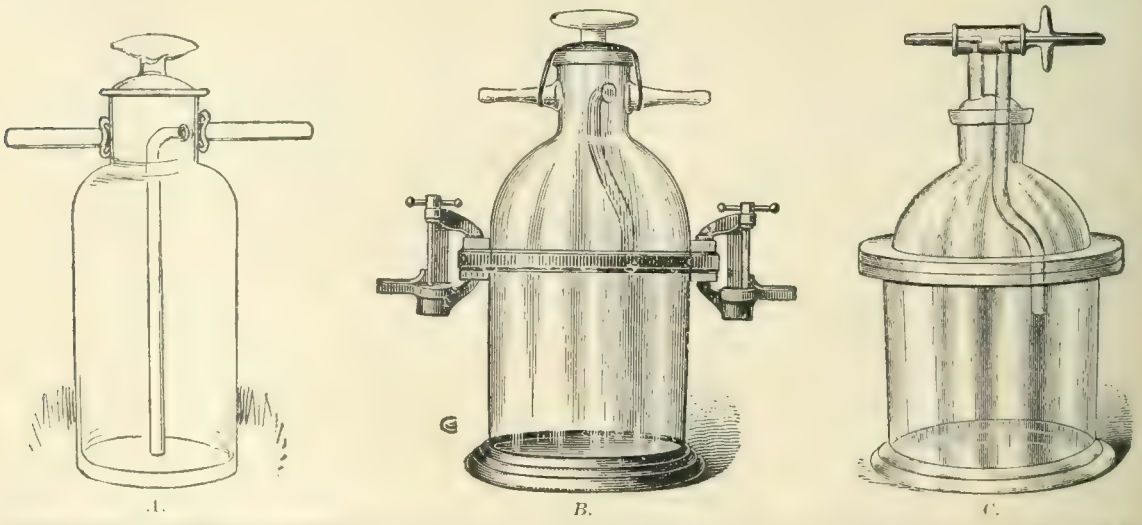


Fig. 5094. Novy Apparatus for Anaerobes. *A*, Bottle for tube cultures; *B*, jar for Petri plates; *C*, jar for plates with special stopcock for vacuum culture.

The bottle (Fig. 5094, *A*) is made in two sizes, 8 × 16 and 10 × 20 cm., which dimensions do not include the neck. A piece of cotton should be placed on the bottom. The ordinary test tubes containing any medium are inoculated in the usual way. The cotton plug is then cut off square, and by means of a pair of crucible tongs the tube is lowered into the bottle. It is advisable, if the cotton plug is very tight, to loosen it up by partially pulling it out. A single jar can be filled in this way with a large number of tubes containing either solid or liquid media. The stopper is then put in place and the apparatus connected with a hydrogen generator. When the gas has passed for a sufficient length of time the bottle is closed by giving the stopper a turn. As will be seen this jar can be used likewise for the pyrogallate method.

The plate apparatus shown in Fig. 5094, *B*, consists of two parts. The inner dimensions of the lower part are 12 × 12 cm. The Petri plates are stacked into this compartment. The flanges are covered with a mixture of beeswax and olive oil (1:4). The two parts are then brought together and a rubber band is slipped over the outer edge of the flanges. Two or three clamps or small vises are now applied. The jaws of these should be covered with a piece of rubber tubing. Gas is passed as in case of the bottle, and at the conclusion of this operation the stopcock is given a turn so as to seal the apparatus.

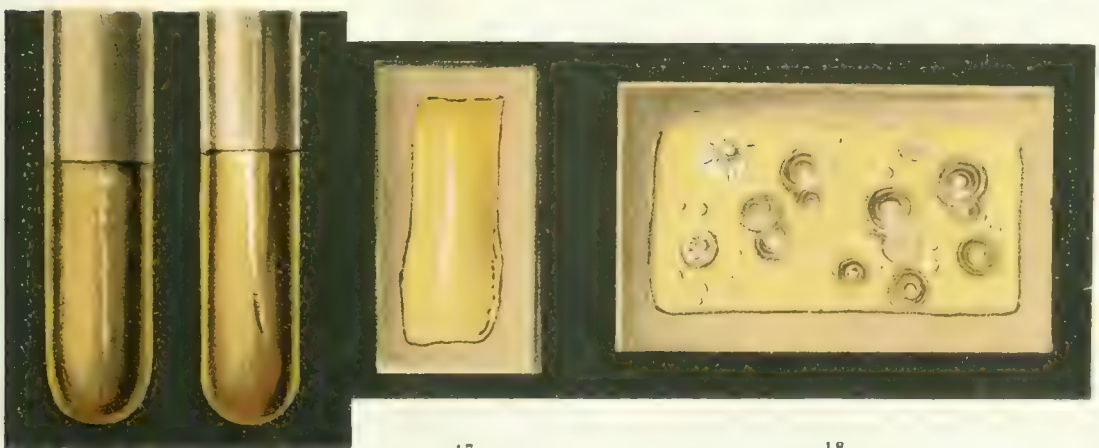
The other modification (Fig. 5094, *C*) has a special stopper, which enables it to be used for vacuum cultures. It can, however, be employed equally well for hydrogen cultivation. Moreover, both forms of the plate apparatus, as well as the bottle, can be used for the pyrogallate method.

3. *Absorption of Oxygen.*—The most convenient absorbent for this purpose is an alkaline solution of pyrogallic acid. The principle was first utilized by Buchner for tube cultures, as shown in Fig. 5095. The large outer tube is provided with a closely fitting rubber stopper. On the bottom of the tube is placed about a gram of pyrogallic acid and a suitable support. The tube containing the nutrient medium is inoculated in the usual way and placed on this support. Finally 10 c.c. of a ten-per-cent. solution of potassium or sodium hydrate is added from a pipette, as rapidly as possible, and the tube is then quickly closed with the stopper.

As mentioned above, the Novy apparatus can be employed for the pyrogallate method. In the case of the jar a wide tube is introduced which contains about 2 gm. of the acid. After the culture tubes have all been inserted, about 20 c.c. of a twenty-five-per cent. solution of sodium hydrate is introduced into the pyrogallate tube

1. Bacillus of Tuberculosis.
2. Bacillus of Cholera Asiatica.
3. The same in gelatine.
4. Finkler-Prior's Comma Bacillus.
5. Deneke's Bacillus
6. Miller's Bacillus.
7. Bacillus of Typhoid Fever.

8. Pneumococcus.
6. Bacillus of Glanders.
10. Bacillus of Anthrax.
11. The same in gelatine.
12. Bacillus of Malignant Oedema.
13. Bacillus of Septicaemia of Mice.
14. Bacillus of Septicaemia of Rabbits.



15. Bacillus of Chicken Cholera.
16. Bacillus of Pigeon Diphtheria.
17. Slide Culture (reduced).
18. Plate Culture (reduced.)

TEST-TUBE CULTURES.

Reproduced from Huber & Becker's "Untersuchungs-Methoden."

from a pipette, and the stopcock is then inserted as quickly as possible and turned. In the case of the plate apparatus a crystallizing dish, about 10 cm. in diameter and about 2 cm. high, is placed on the bottom, and about 4 gm. of pyrogallic acid added. A couple of strips of glass are then placed on top, and on these are stacked the Petri dishes. Twenty-five cubic centimetres of the strong alkali are introduced in the manner just mentioned, after which the top is put into place, the clamps and the rubber band are applied.

FIG. 5095.—Buchner's Pyrogallate Method.

Wright's method will be found to be very useful for occasional cultures. The cotton plug is cut off square and pushed down about 1 cm. into the tube. The plug is made of absorbent cotton. It is then moistened with about 4 c.c. of a strong solution of pyrogallic acid, after which about the same volume of strong sodium hydrate (1:2) is added. The tube is closed as rapidly as possible with a tight-fitting rubber stopper. Obviously, solid pyrogallic acid may be used.

It will be seen that the pyrogallic-acid method is extremely convenient and very simple, requiring a minimum of time and expense. The method is also applicable for the *hanging-drop examination* of anaërobic bacteria. A drop of alkali and of the acid can be placed on the side of the concave slide. After the cover is in place the slide can be tilted so as to bring the two liquids together. A special slide for this purpose was devised by Braatz (Fig. 5096).

The hanging drop is made and placed over the well. The flat flask contains the pyrogallic acid and communicates with the space below the drop. Strong alkali is finally added and the flask is closed with a stopper. Pyrogallic acid can also be employed in connection with Hill's "hanging-block" culture. Another apparatus for anaërobic hanging drops is that of Kühne. It is very serviceable and can be used for either the gas or pyrogallate process.

4. *Exhaustion of Air.*—Pasteur employed **U**-shaped tubes, from which the air was removed by means of an air pump. Gruber applied the principle to the tube culture. He used a stout glass tube, which was provided with a stopper, through which passed a short glass tube by which connection was made with the air pump. The test tube was constricted just below the stopper so as to facilitate the subsequent sealing process. The tube was filled in the usual way with the nutrient medium and inoculated. It was then connected with the pump, and as soon as the air was exhausted the tube was sealed at the constriction. The plate apparatus shown in Fig. 5094, *C*, is intended for vacuum as well as gas or pyrogallate cultures. It can be used for tube or plate cultures.

5. *Mixed Cultures.*—This method of cultivating anaërobic bacteria corresponds to the way in which these organisms grow in nature. If the anaërobe is planted together with an aërobe, the latter will consume all the oxygen in the immediate neighborhood, and as a result the anaërobe will grow. Thus, if the tetanus and hay bacilli are planted at the same time into a tube of bouillon, they will both develop. Other aërobic bacteria, such as the Bacillus prodigiosus and Proteus vulgaris, can be used for the same purpose.

6. *Cultivation in Air.*—This of course is apparent rather than real. If a tube of glucose gelatin, preferably colored with litmus, be inoculated with an anaërobe and then set aside in the incubator, an abundant growth will develop (Novy's method). Similarly, when deep stab cultures are made of the anaërobes, it will be found quite frequently that the water of condensation on the top of the medium is cloudy from the growth of the germs. The explanation in the one case is that air is excluded partly by the viscosity of the liquid and partly by the evolved gases. The gas formation accounts for the growth of the germs in the water of condensation. The culture in glucose litmus gelatin is by far the simplest way of growing anaërobes. Moreover, the cultures thus obtained retain their vitality for many years. In some cases the author has recovered cultures from tubes five and six years old.

Collodium Sacs.—This method of cultivating has been used extensively by the Pasteur School for exalting the virulence of bacteria. The underlying idea is to grow the organisms in the peritoneal cavity of an animal, and under such conditions that the waste products of the germs will be removed, an abundant supply of nutrient material furnished, and the germs themselves protected against the action of phagocytes. This is accomplished by enclosing the bacteria in a hermetically sealed sac, the walls of which are permeable to the waste products of the germs and to the soluble proteids of the peritoneal fluid. Several Russian workers have employed for this purpose the inner lining membrane of reeds, but the best procedure is to make the sacs of collodium. Various methods have been devised for the rolling of the sac, but undoubtedly the best and simplest is that perfected in the author's laboratory by Gorsline.

The rolling tube employed for making sacs is about twelve to fifteen inches long, and of any width that may be desired. For ordinary purposes a width of half an inch is sufficient. One end of this tube is rounded off like a test tube, and has a 2 mm. opening at the tip. This opening is first closed with collodium either by touching it with the cork which has been covered with the solution, or the collodium may be applied with the finger. Care must be taken to see to it that the collodium does not get inside of the tube. In a few seconds the layer is dry enough to go ahead.

The collodium used is the United States Pharmacopœia solution, which by exposure to the air has been concentrated by one-third or one-half. It should be perfectly clear, and if not it must be filtered through cotton by the aid of a pump. The collodium can be kept in a glass-stoppered cylindrical vessel, such as is used for the collection of blood. The collodium is inclined till it comes within a few inches of the opening.

The rolling tube, with the opening freshly closed, is dipped in the collodium and rolled several times in the liquid. It may be rolled so that only the lower side of the tube touches the collodium. If the sac is to be very thin it is sufficient to roll the tube but two or three times, after which it is raised from the liquid and rolled in the ether atmosphere in a horizontal position till the collodium has set. If the layer is not thick enough the tube can be returned to the collodium, but care must be taken

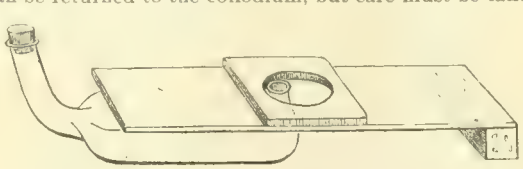


FIG. 5096.—Braatz's Slide for Anaërobic Hanging-drop Examinations.

to avoid the formation of air bubbles. The coated tube is finally rolled in the air until it has reached the proper consistence. This can be ascertained by touching the thickest part with the finger. The collodium layer should be rather firm. The tube is then immersed in distilled water for a minute or two. If the collodium is not sufficiently hard, it will cloud or become milky on contact with the water. It should remain perfectly clear, and when finished a thin sac placed in water is almost invisible.

To detach the sac the tube is filled with distilled water, and by blowing into the open end the water can be forced through the opening below and upward between the sac and the tube. By slight manipulation with the fingers the detachment can be effected readily on all sides. The free end is then trimmed square, after which the sac is placed in distilled water, where it remains until it is ready to be attached to the glass tube.

An ordinary test tube having a diameter slightly less than the sac is constricted in the blast flame at about two inches from the end. A scratch is then made, about a half an inch below the constriction, with a diamond, and with the aid of a hot rod the end is removed. The resulting tube has the form shown in Fig. 5097, *a*. The cut end should be rounded in the flame so as to remove the sharp edge.

The inside of the neck of the sac is dried by means of filter paper, after which the end of the tube is inserted. This can be done more easily if the end of the tube is previously dipped in alcohol. The next step, that of shrinking the sac upon the tube, is very important and requires care. Most of the shrinking is done by rotating the tube, in a horizontal position, some distance above a small spare-flame burner. In this way the collodium can be made to contract down upon the glass, but the operation must be done slowly and at some distance above the flame, otherwise there is danger of igniting the sac. The adhesion is rendered more complete by the application of a hot glass rod. Finally a silk thread is wound as closely as possible over the glass neck, and this in turn is covered with a layer of collodium. The sac now has the appearance shown in Fig. 5097, *b*. The finished sac is now filled with distilled water and placed in a test tube on foot, which also contains water (Fig. 5097, *c*), and the whole is sterilized by steaming in an autoclave for half an hour at 110°.

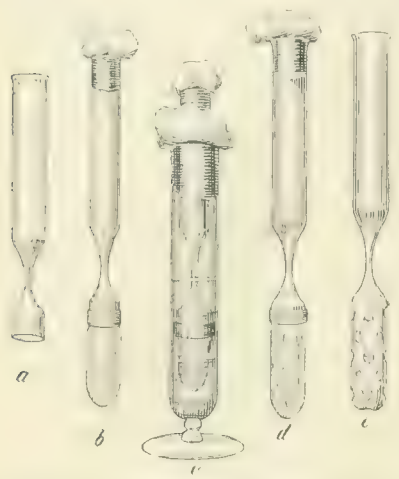


FIG. 5097. Preparation of Collodium Sacs (Novy.)

When the sac is to be used, the water is removed from the inside by means of a drawn-out pipette and refilled in like manner with bouillon which has been inoculated with the organism to be tested. The threaded part is then wrapped in a piece of sterile filter paper, for convenience in handling, and the constriction is sealed in a sharp-pointed flame. The sealed sac is then placed in a sterile test glass.

The rabbit or guinea-pig which is to receive the sac is now attached to a holder and the hair is removed from the abdomen. The field of the operation is thoroughly washed with lysol or mercuric chloride. After the animal is anæsthetized an incision is made in the abdominal wall, and through this the sac is introduced into the peritoneal cavity. The incision is then sewed up and covered with cotton and a little collodium.

The sac is allowed to remain in the animal for a few days or even for several months. To remove it the animal is killed with gas. The sac is freed from the adhesions and transferred to a sterile test glass with the glass end downward. By means of a hot rod an opening is burned into the end of the sac, and through this the contents are removed by means of a drawn-out tube pipette. When large sacs are to be inserted into an animal it is advisable to strengthen

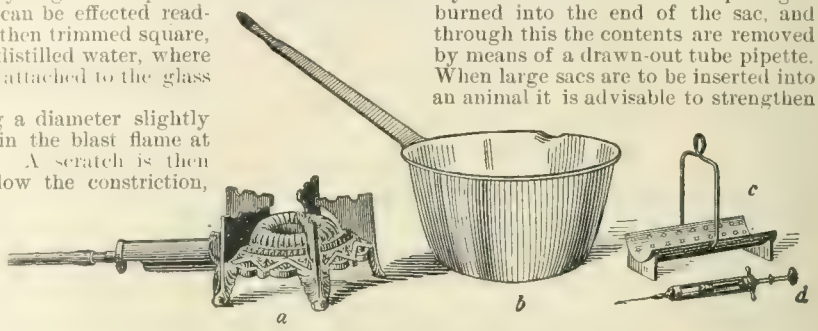


FIG. 5098.—Syringe Holder and Sterilizing Pan. (Novy.)

these by placing within a perforated glass tube as shown in Fig. 5097, *e*, *f*.

The collodium sacs can be used not only as just described, but also with marked advantage for dialyzing experiments. For this purpose the sacs can be made an inch or more in diameter and twelve or fifteen inches long. The thin collodium membrane is considerably more permeable than parchment paper.

INOCULATION OF ANIMALS.—According to the nature of the experiment these are made with pure or impure cultures of bacteria, or with the chemical products elaborated by them. The use of impure material is met with in diagnostic work. Thus in suspected glanders the discharge is introduced into animals in order to ascertain if the bacillus of glanders is present. The same is often done in tuberculosis, pneumonia, bubonic plague, anthrax, tetanus, rabies, etc. In all these experiments the animal serves as a plate, since it eliminates all the saprophytic bacteria which may be present in the original material and allows the disease-producing ones to develop in pure or almost pure cultures. The inoculation with pure cultures is made to test their identity, to study their effects upon animals, and to ascertain the diverse means of infection, and for purposes of immunization. The inoculation with the chemical products serves to ascertain the presence of poisonous substances, or to produce vaccines or antitoxins.

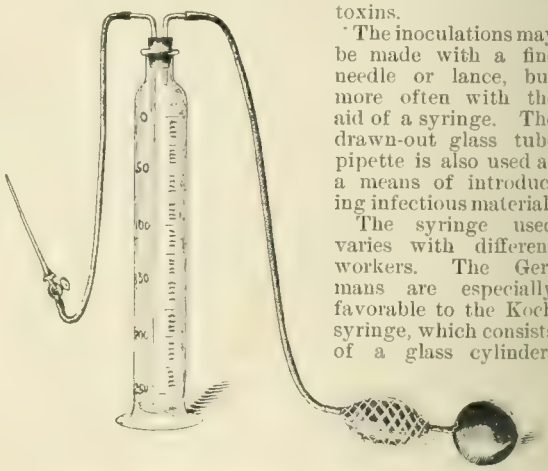


FIG. 5099.—Graduated Cylinder for Injecting Liquids. (Novy.)

The inoculations may be made with a fine needle or lance, but more often with the aid of a syringe. The drawn-out glass tube pipette is also used as a means of introducing infectious material.

The syringe used varies with different workers. The Germans are especially favorable to the Koch syringe, which consists of a glass cylinder, graduated, the narrow end of which connects with the needle while the upper end fits into the metal collar of a rubber bulb. The advantage claimed is that the cylinder and needle can be effectively sterilized by dry

heat. As a matter of fact the Koch syringe is extremely inconvenient and unsatisfactory, and equally good results with less time and annoyance are obtainable with the ordinary hypodermic. The latter of course must be sterilized by boiling in water for ten or fifteen minutes. A convenient holder for the syringe is shown in Fig. 5098.

When large quantities of liquids are to be introduced, as when injecting horses with diphtheria toxin in the preparation of antitoxin, an apparatus similar to that shown in Fig. 5099 can be used.

The necessary instruments, such as knives, scissors, needles, etc., are sterilized by boiling in water, or better in a saturated solution of borax. A very convenient sterilizer for this purpose is that shown in Fig. 5104.

In all operations the animal must be secured in some way or another. Various kinds of holders have been constructed for this purpose. That of Latapie, shown in Fig. 5100, is very convenient, and is to be preferred to the ordinary models. It can be used for guinea-pigs, rabbits, birds, etc.

The Voges holder, shown in Fig. 5101, is useful for taking temperatures and for injecting small animals. A good substitute can be made by using a glass cylinder,

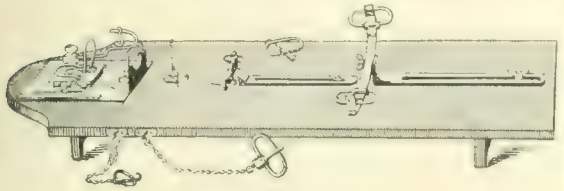


FIG. 5100.—Latapie's Animal Holder. (Novy.)

Special holders have been devised for rats and mice. These, however, can be handled best by means of a pair of compression or artery forceps. The animal is seized by the nape of the neck with the forceps, which are then transferred to the left hand. The tail and the hind legs are also held by this hand. The animal in this way is put upon the stretch, and the inoculation can then be made with the right hand. Even full-grown wild rats can be handled in this way without the help of an assistant.

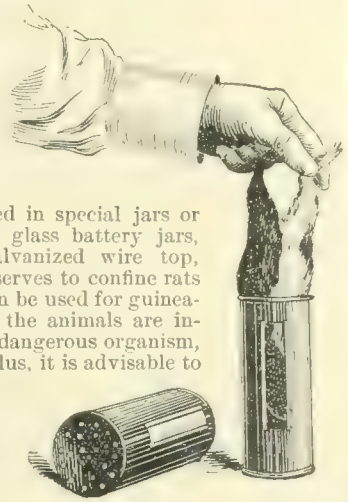


FIG. 5101.—Voges' Holder for Small Animals. (Novy.)

After inoculation the animals are placed in special jars or cages. The ordinary glass battery jars, provided with a galvanized wire top, weighted with lead, serves to confine rats and mice, and can even be used for guinea-pigs (Fig. 5102). If the animals are inoculated with a very dangerous organism, such as the pest bacillus, it is advisable to place the jar inside of a ten-gallon crock. In special cases, as in animals infected with trypanosomes, bubonic plague, etc., it is well to cover the cage with a piece of mosquito netting as a safeguard against insects spreading the infection.

Guinea-pigs, rabbits, and the like can be kept in the Vaughan cage shown in Fig. 5103. The cage proper is 30 cm. high, 38 cm. deep, and 54 cm. wide. The feet are 12 cm. high.

1. *Cutaneous Application.*—Ordinarily bacteria do not penetrate the unbroken skin or mucous membrane. The direct application of some organisms, even in the absence of any known lesion, leads to infection. This is the case when the virus of the foot-and-mouth disease or the bacillus of plague is brought into contact with the mucous membrane. The pus germs, when rubbed into the skin by the aid of vaseline, may cause infection.

2. *Subcutaneous Application.*—For this purpose the hair is removed from the region where the inoculation is to be made. The place is then rubbed with a disinfectant. In the rat this is usually on the back, at the root of the tail; in the guinea-pig it is on the side. A nick is made with sterile scissors, and then with a narrow scalpel or spatula a pocket is made under the skin. A piece of tissue, a bit of earth, blood-laden wire, etc., is then introduced into the opening, which if made small requires no special closure.

FIG. 5102.—Rat Cage and Forceps. (Novy.)

3. *Subcutaneous Injection.*—The suspended material is introduced under the skin by means of a syringe. The hair should first be clipped close and the place of inoculation touched up with a disinfectant.

4. *Intravenous Injection.*—In the case of the rabbit this is easily done. The marginal branch of the posterior auricular vein is selected, although it may appear to be narrower than the needle. The hair may be removed and the surface of the ear rubbed freely to stimulate circulation. A clamp is then applied at the base of the ear so as to distend the vein. The needle is then inserted at a very slight angle to the vein. In other animals the jugular can be exposed and the injection made without any difficulty. In the preparation of preventive sera the culture or toxin is often injected into the jugular of a horse. A trocar is first introduced into the jugular, and this is then connected with the cylinder containing the liquid to be injected (Fig. 5099).

5. *Intraperitoneal Injection.*—This procedure is very commonly resorted to. The skin over the abdomen should be raised and the needle of the syringe is then introduced into the cavity. In the case of the horse, while the animal is standing, a trocar is introduced through the skin at a point a few inches anterior to the crest of the ilium.

6. *Intrapleural Injection.*—The needle is introduced into the right pleural cavity, care being taken to prevent

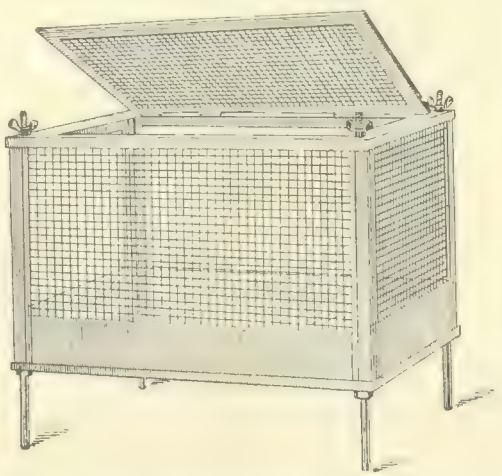


FIG. 5103.—Vaughan Cage. (Novy.)

any injury to the lung or to the heart. Large amounts of liquid cannot be tolerated by the animal.

7. *Intracranial Injection.*—This method was introduced by Pasteur as a means of surely infecting animals with rabies. The procedure is followed out when inoculating animals either for diagnosis or for the purpose of preparing the vaccine for hydrophobia. It is usually practised on rabbits and guinea-pigs. The skin from between the ears forward is shaven clean and disinfected. An incision about an inch long is then made. The Pasteur School apply a hand trephine, and make an opening into the skull. A small trephine, operated by a dental engine, is much more convenient. In the absence of either an opening may be made into the skull with a stout scalpel. By means of a hypodermic syringe a few drops of the brain or cord suspension are then introduced under the dura. At times the injection is made into the brain proper, in which case it is spoken of as *intracerebral*. After the injection a suture or two is applied, and the wound is covered with collodium and cotton.

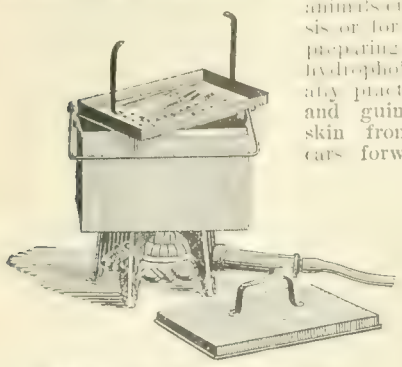


Fig. 5104. Instrument Sterilizer. Novy.)

8. *Intra-ocular Injection.*—Cocaine is first applied to the eye, after which this is fixed with forceps and the material injected into the anterior chamber. If desired, an opening can be made with a cataract knife or narrow scalpel and the solid material can be introduced in this way.

9. *Injection into the Lymphatics.*—This is usually made by introducing the material into the testicles.

10. *Respiratory Infection.*—While the preceding methods may be looked upon as wound inoculations, this concerns itself as nearly as possible with duplicating the natural infections along the respiratory tract. The direct method consists in causing the animal to inhale the finely divided material, which can be readily done by means of an atomizer. Another procedure may be called the *intratracheal* injection. This is carried out by making an opening into the trachea, and through this introducing the infectious agent.

11. *Alimentary Infection.*—Since water and food serve to introduce the pathogenic agent of many diseases into man and animals, it is necessary at times to resort to a similar method of infection. The animal may receive the infectious agent in water, milk, or in solid food. Thus

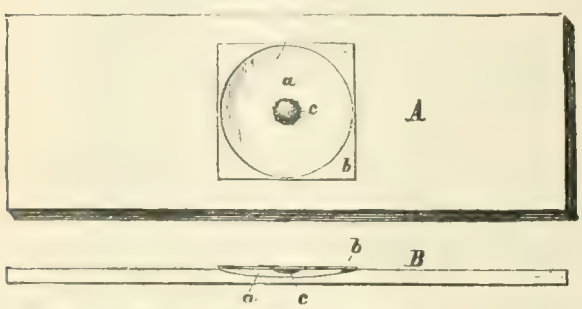


Fig. 5105. Concave Slide showing Hanging Drop. *A*, Surface view; *B*, side view.

bread may be soaked in a bouillon culture of the organism. At other times it may be necessary to introduce the material into the stomach by means of a rubber tube. In order to prevent the animal from biting the tube, it is well to pass it through a perforated cork or plug of soft wood. Under exceptional conditions a laparotomy may be made and the material injected into the intestines. This is spoken of as the *intraduodenal* injection.

Observation and Autopsy of Infected Animals.—The matter of suitable caging of animals has already been touched upon. Attention may be called to the need of daily observations of the infected animals, so as to note the symptoms manifested. The animals must have plenty of food and drink, and must be kept in as clean a condition as possible. Their weight and temperature should be taken daily, for in this way the best information can be gained as to the physical condition of the animals.

When the animal dies it should be autopsied at once, or else it must be put aside in an icebox. The need of immediate examination is shown in some of the trypanosomatic infections, as nagana and caderas, where the organism may disappear from the blood within an hour or so after death. Moreover, delayed examination may lead to the invasion of the organs of the cadaver by the intestinal bacteria, in which case the search for the specific germ is rendered more difficult, if not impossible.

The animal is prepared for autopsy by being placed on its back and tacked down on a board. A convenient board of this kind is one which is about 34 by 54 cm., and has a raised border. The cracks, if any, should be filled with paraffin.

After the animal is laid out, the hair should be thoroughly moistened with mercuric chloride solution. The

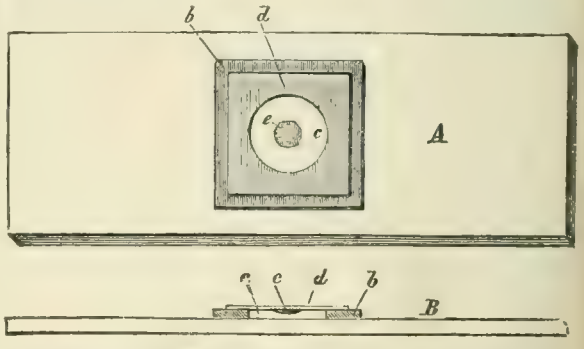


Fig. 5106.—Cell Slide showing Hanging Drop. *A*, Surface view; *B*, side view; *b*, edge of cell; *c*, hollow of cell; *d*, cover glass; *e*, hanging drop.

necessary instruments can be sterilized in a copper sterilizer, such as is shown in Fig. 5104. In the absence of such an arrangement the instruments may be sterilized by heating directly in the flame, but this, of course, injures them. A searing iron, several drawn-out pipettes and sterile dishes, as well as the necessary media, should be conveniently on hand

With a sterile scalpel an incision is made along the entire length of the body from the neck to the pubis. Lateral incisions are then made in the direction of each of the extremities, and the two large flaps thus resulting are turned back. The condition of the subcutaneous tissue, the presence of œdema, bloody effusions, enlarged lymphatic glands, etc., are noted. The glands or portions of the tissues may be transferred by means of sterile instruments to a sterile dish. Cover-glass smears or streaks can be made and examined either at once or later.

The abdominal and thoracic cavities are usually opened at the same time. The abdominal wall in the lower part of the body is slightly raised and nicked with sterile scissors; then the lower blade is inserted and the incision prolonged upward to the diaphragm. The ribs are then cut as low down as possible, and the wedge-shaped piece of the wall of the thorax is removed. The condition of both cavities and of the organs is carefully noted. Cover-glass streaks are made from the peritoneal surfaces and from the cut surfaces of the organs, and examined either at once or later. Any fluid which is present in

the cavities may be transferred to sterile tubes by means of the pipette.

Cultures should always be made from an intact organ. For this purpose it is cut open with sterile scissors, and a piece of the pulp removed on a sterile wire, or by the aid of a Nuttall spear or spatula (Fig. 5083). The heart blood is usually given preference for culture purposes. The pericardium should be opened, after which the surface of the heart is seared with a hot iron. An incision is then made into the ventricle, from which the blood can be removed by the aid of a looped wire. The best way of removing the heart blood is by means of a sterile Pasteur bulb pipette. The end of this is broken, flamed, and when cool it is inserted into the heart, and by suction the blood is drawn up into the pipette. The contents of the tube can then be used to inoculate culture media or for making blood streaks.

After the autopsy the animal should be placed in a vessel and steamed or autoclaved, and eventually burned. The board should be washed with mercuric chloride, and all instruments and utensils should be sterilized by steaming. Throughout the autopsy care must be taken to prevent infection, either by scattering the material on the floor or by its being carried away by insects.

Examination of Bacteria.—In order to gain some definite information regarding the bacteria which develop on the nutrient media, or in the animal body, recourse must be had to the microscope. The organisms may be examined in the living condition or in stained preparations. The former procedure is resorted to so as to learn all that is possible regarding the living cell: its form, size, color, granulations if any, motion, grouping of the cells, presence of spores, etc. Such facts are ascertained by making a preparation in which the bacteria will continue to live for some time.

Living Bacteria.—1. The simplest procedure is to place a drop of the bacterial liquid on a slide, after which the cover-glass can be applied and the preparation examined under the microscope. This method is useful for rapid orientation, but it has certain drawbacks, chief among which is the fact that evaporation takes place along the edge of the glass, and as a result currents are established in the liquid. Such currents tend to interfere with the observation of any one organism or group of cells. Again, a preparation of this kind cannot be kept under observation for any length of time on account of the desiccation which soon takes place.

2. The examination in a hanging drop, as it is called, obviates the difficulties mentioned. A rather thick slide with a concave well is used (Fig. 5105). A ring of vaseline is spread around the edge of this well. A clean cover glass, about three-fourths of an inch in diameter, is placed on the table, and a drop of water is applied to the middle by means of a looped platinum wire. It is desirable that the drop should spread out flat, and if it does not it is because the cover glass is not clean. The drop of water is then inoculated with a little of the culture. Just enough material is added so that the liquid is slightly cloudy. The vaseline-ringed slide is then inverted and brought down upon the cover glass. The preparation is turned over, and, if need be, pressure applied to the border of the glass so as to have an air-tight hanging drop. Under these conditions evaporation does not take place, and consequently the specimen may be examined for hours, if necessary, without any interference by currents due to evaporation. As mentioned above, this method can be used for the cultivation of bacteria, and thus their growth and multiplication can be followed out. In that case it is necessary to use a flamed cover glass and a sterile liquid.

Instead of the concave slide a so-called well slide can be used (Fig. 5106). This is essentially a square bit of glass with a circular opening which is cemented to an ordinary glass slide, and the hanging drop is then made in the manner described.

One disadvantage in either method lies in the fact that the drop is more or less convex, and consequently when using higher powers it is difficult to examine the deeper portions. This difficulty can be overcome by employing the Ranvier slide, which has a circular trough, and the portion within the circle is ground down so that its level is about 0.1 mm. below that of the slide. When a drop of liquid is placed within the circle and covered with a cover glass, the liquid spreads out into a thin layer, every part of which can be examined under the microscope. A ring of vaseline is placed along the edge so as to prevent evaporation. By flaming the slide and cover slip and using sterile liquid the preparation can be observed for several days if need be. This method is especially to be recommended for studying trypanosomes, malaria parasites, etc.

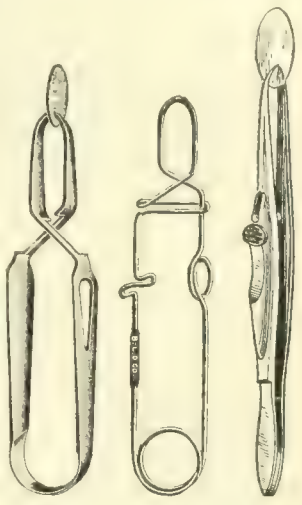


Fig. 5107.—Cover-glass Forceps. *a*, Cornet's; *b*, Stewart's; *c*, Novy's.

Staining of Bacteria.—In order to obtain good stains it is necessary to have good clean cover glasses. The cover slips, as purchased in the market, are unfit for use until they have been cleaned. One method of doing this is to heat the slips in a beaker with concentrated sulphuric acid and potassium bichromate. The cover glasses are then washed in running water, after which they are kept in alcohol. Another procedure which gives very satisfactory results is to soak the cover glasses first in alcohol, after which they are wiped with soft, washed linen, placed in an Esmarch dish and heated in a dry-heat sterilizer at about 200° for an hour or two. This high heat completely destroys the organic matter that may be on the glasses. A cover glass is not clean if a small drop of water, when spread over the surface, does not remain even but gathers into droplets.

Several kinds of forceps have been devised for holding cover glasses while staining. The Cornet forceps (Fig. 5107, *a*) are well known, and are useful though rather awkward. Stewart's modification is widely used (Fig. 5107, *b*). A much more convenient forceps is shown in Fig. 5107, *c*. The lower blade has a thin edge which permits one to pick up the cover glass without contact with the fingers. The upper blade is bent in order to avoid capillarity, and is narrowed to a point so that the specimen is held by point contact. A catch serves to hold the cover slip in place.

Aniline Dyes.—The aniline dyes which are employed for staining purposes are either basic or acid in character. The former contain amido groups and are spoken of as nuclear stains, since they color the nuclei of cells as well as bacteria. The latter contain hydroxyl groups and do not stain bacteria, but are used chiefly for contrast coloring, and to some extent for decolorizing. The basic dyes are usually employed as salts of hydrochloric acid, while the acid dyes occur as sodium or potassium salts.

Among the basic aniline dyes which are commonly employed may be mentioned fuchsin, gentian violet, methyl violet, crystal violet, methylene blue, thionin, safranin, methyl green, neutral red, and vesuvin or Bismarck brown. These are all more or less crystalline powders, and while some are definite chemical compounds, others are mixtures. For this reason various brands are met with on the market, and it will be readily understood why the exact duplication of stains is not always possible.

It is advisable to keep on hand not only the solid dyes, but also stock solutions which are saturated alcoholic

solutions. The amount required to saturate will vary from two to five per cent.

The concentrated alcoholic solutions are never used as such, but serve for the preparation of the dilute dyes which are the stains proper. The latter are made by

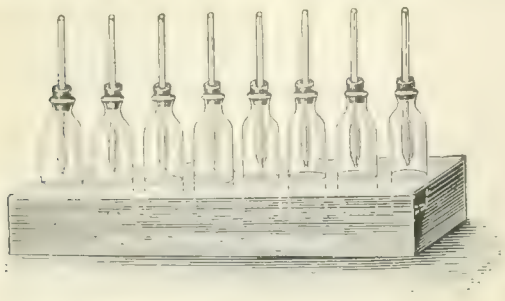


Fig. 5108. Stand for Staining Solutions.

placing a few cubic centimetres of the concentrated dye in a small tincture bottle, and adding ten to twenty parts of water. This bottle is then provided with a cork and a piece of glass tubing which serves as a pipette. The different dilute dyes can be kept in a stand, such as is shown in Fig. 5108. The dilute dyes after a while undergo alteration and yield deposits. In that event they should be filtered before use, or else new dilutions should be made.

The acid aniline dyes are represented by eosin, acid fuchsin, and fluorescein. The concentrated and the dilute dyes are prepared as above.

The staining solutions may be used as such, or their properties may be accentuated by the addition of substances which act more or less directly as mordants. A number of these solutions are in daily use, and for that reason their preparation is here given.

Löffler's methylene blue is made by adding 30 c.c. of concentrated methylene blue to 100 c.c. of a 0.01-per-cent. solution of potassium hydrate. A similar solution with less alkali was first used by Koch. The alkali not only serves to make the cell more permeable, but also increases the staining power by liberating the free base from the dye.

Carbolic fuchsin, or Ziehl solution, is made by adding 1 gm. of fuchsin and 10 c.c. of alcohol to 100 c.c. of a five-per-cent. carbolic-acid solution. This stain is very widely used for simple as well as double staining. Czaplewski modified it by substituting glycerin for the alcohol. His solution is prepared by rubbing up in a mortar 1 gm. of fuchsin with 5 gm. of carbolic acid, and to this 150 gm. of glycerin and 100 c.c. of water are added.

Carbolic methylene blue, first employed by Kühne, consists of 1.5 gm. of methylene blue, 10 gm. of absolute alcohol, and 100 c.c. of a five-per-cent. solution of carbolic acid.

Carbolic theonin consists of 10 parts of a saturated solution of thionin and 100 parts of a one-per-cent. solution of carbolic acid (Nicolle).

Carbolic gentian violet is made the same as the preceding (Nicolle).

Aniline Water, Gentian Violet, etc.—The carbolic acid, like the alkali, favors the penetration of the stain. Aniline water acts in like manner and was first used by Ehrlich. To prepare the aniline water a few cubic centimetres of aniline are placed in a test tube, and this is then filled with distilled water and thoroughly shaken. The milky liquid is filtered through a moist filter. To the water-clear filtrate enough concentrated fuchsin or gentian violet is then added to make the liquid opaque, and so that it just begins to form on the surface a slight metallic film of precipitated dye. The solution is then used as such, but if the deposit is very marked it may be necessary first to filter it. The aniline water dyes do not keep very well, and for that reason it is well to make a fresh solution every time that it is to be used. Oil of cloves has been suggested by London as a substitute for aniline.

The aniline water stains were first employed by Ehrlich for coloring the tubercle bacillus, and are still used for that purpose. They are, however, employed especially for staining whips and in connection with Gram's stain. In the latter case, after the preparation has been stained with the solution, a mordant is applied, known as Lugol's solution, which serves to form a difficultly soluble compound between the dye and the cell contents.

Lugol's solution consists of 1 part of iodine, 2 parts of potassium iodide, and 300 parts of distilled water.

The Staining of Cover-glass Preparations.—These may be considered under the head of (1) simple, (2) double, and (3) special stains. For the simple stains, when it is desired to have a heavily colored preparation, either fuchsin or gentian violet is used. When it is desired to bring out structural characteristics, it is advisable to employ solutions which stain more feebly, such as methylene blue or thionin. In either case the simple or reinforced stains, given above, may be employed.

To make a stained preparation of a pure culture the procedure is as follows: A drop of water, preferably distilled, is placed upon a clean cover glass, which either lies on a board or is held in a pair of forceps. By means of a sterile platinum wire a minute amount of the bacterial growth is picked up and transferred to the water. Only enough should be added so as to impart to the water a slight cloudiness. The remainder on the wire is then burned off. The drop is then spread over the whole surface of the glass and allowed to dry in the air, or the process may be hastened by passing it above a flame. The air-dried preparation must now be fixed in order that the bacteria are not washed off in the subsequent treatment. The fixing is done by passing the cover glass three times through a flame. Care must be taken not to scorch the specimen, for in that case the dye will not act. It is well to turn down the flame so that it is at most but two inches high. The properly fixed cover glass is now covered with the stain, which is allowed to act for ten to twenty seconds. The dye is then washed off under the tap and the cover glass inverted upon a glass slide. Any water which may be on the surface of the slip should be removed by means of a piece of filter paper. The preparation can now be examined under a No. 7 objective, or with the one-twelfth inch oil immersion lens. If the specimen is such as to merit preservation a drop or two of water may be applied to the edge, and in this way the slip can be floated off without damaging the film. The excess of water can then be touched off with a piece of filter paper, after which the specimen is dried in the air or by passing it over the flame. The thoroughly dried film is then inverted upon a drop of Canada balsam placed on the centre of a clean slide. By gentle warming or by pressure the balsam can be made to spread out evenly.

Smear or streak preparations made from the fluids or organs of the body are stained in the same way. The fixation of the cover glass when it contains much proteid matter, as in the case of blood streaks, requires special care. The best results are obtained by immersing the slip for a few minutes in a mixture of equal parts of absolute alcohol and ether. Fixation is thus accomplished without any injury to the blood cells. It is sometimes advisable instead of adding the dye to the cover glass to float the latter upon the dye in a watch glass.

To make good blood preparations requires considerable care and experience. A small drop of blood is placed on a perfectly clean cover glass, which is held in a pair of forceps. A second cover slip is then applied, evenly and without pressure, and as soon as the blood has spread out the two glasses are drawn apart. The blood cells must not be crushed and should lie in a single layer.

The smears from the cut surface of an organ are made by gently applying the cover glass, without pressure, and then drawing it away; or a piece of the organ may be taken up in the forceps and streaked over the cover

glass, care being taken to leave only the thinnest film possible.

The ordinary glass slide is often used in place of the cover glass. The streaks or blood smears are made as in the case of the latter. When the growth is hard, as in the case of actinomyces, it is well to crush it between two glass slides.

Double Staining.—This procedure is resorted to when staining the tubercle bacillus and the allied acid-resisting bacilli. It is also used for staining spores, and in differentiating bacteria by means of Gram's stain. Other special methods are given under gonorrhœa and meningitis.

The group of acid-resisting bacilli, the type of which is the tubercle bacillus, are stained with more or less difficulty by the simple stains. The dye, however, can be forced into the cell by the aid of heat, and especially if the reinforced stains, such as carbolic fuchsin or aniline water gentian violet, are used. On subsequent treatment with acid and alcohol the ordinary bacteria, which chance to be present, are readily decolorized, whereas the acid-resisting retain the stain. A contrast color, such as methylene blue, will then stain the background and the ordinary bacteria a light blue.

Staining of the Tubercle Bacillus.—The cover glass is air-dried and fixed in the usual manner, after which any one of several methods may be used. The *Ziehl-Neelsen* method is usually employed. It is carried out as follows. The cover glass, held in the forceps, is covered with carbolic fuchsin and heated over the flame so that vapors are given off for one or two minutes. It is then rinsed in water and dipped for a few seconds in a twenty-per-cent. solution of nitric acid, after which it is washed in dilute alcohol (sixty per cent.) till it is almost colorless. Methylene blue is then applied for a few seconds and washed off. The specimen is transferred to a slide, the surface dried, and examined under the microscope. The tubercle bacilli will appear red on a blue background. The ordinary bacteria will appear blue.

The *Koch-Ehrlich method* consists in staining with aniline water fuchsin or gentian violet with the aid of heat for a few minutes. The specimen is then decolored in thirty-five-per-cent. nitric acid for about a quarter of a minute, washed in dilute alcohol till nearly colorless, after which methylene blue or Bismarck brown is applied for a contrast color.

In the *Fraenkel-Gabbet method* the preliminary staining is effected with carbolic fuchsin as above. The decoloration and contrasting is done at once by immersing the cover glass in a saturated solution of methylene blue in the following: Sulphuric acid 25 parts, alcohol 50 parts, distilled water 1,000 parts. It is then rinsed with water and examined.

Czaplewsky's method differs from the preceding in the way the decoloration is effected. He employed for this a solution of 1 gm. of fluorescein and 5 gm. of methylene blue in 100 c.c. of alcohol. The specimen is first stained with carbolic fuchsin; then, without rinsing in water, it is placed for a few seconds in the fluorescein methylene blue solution. Finally it is dipped ten or twelve times in a solution of 5 parts of methylene blue in 100 parts of alcohol. It is then washed with water and examined.

Numerous modifications of these methods have been proposed, but they possess no special advantage over those given.

Staining of Spores.—The cover-glass preparation is treated for some minutes with hot carbolic fuchsin, either on the forceps or by floating on the dye. It should then be rinsed and examined in water. If the spores are colored the next step is taken; if not, then the heating with the dye is continued until they are stained. The specimen is then decolored in dilute acid and alcohol until the spores stand out red on a colorless background. Methylene blue is then applied for a contrast, washed off, and the preparation is ready for examination. The bright red spores are seen within the light blue cells. This method requires considerable care, and every step must be controlled by frequent examinations under the microscope.

In order to enable the dye to more readily enter the spore, Möller treated the cover glass, first, for a minute or two with a five-per-cent. solution of chromic acid, after which essentially the above procedure was followed. By repeated passage through the flame or by heating with strong sulphuric acid for a few seconds the substance of the spore can be disintegrated so that on subsequent staining with carbolic fuchsin the spores will readily take the dye. This treatment, however, destroys the original cell, and hence contrast coloration is not possible.

The Gram Stain.—This is one of the most valuable methods in bacteriology, since it often serves to distinguish between organisms which otherwise resemble each other very closely. The cover-glass preparation is floated for a few minutes on aniline water gentian violet, or on carbolic gentian violet. Heat may be applied, but in that case the excessive staining will interfere with the subsequent decoloration. The specimen is then rinsed in water and immersed in Lugol's iodine solution for two or three minutes. After rinsing in water it is then placed for a few minutes in strong alcohol until most of the dye has been washed out. Very dilute eosin solution is now applied for about five seconds. After thorough washing with water it is ready for examination. The organism will appear a deep violet on a pink background.

Gram's method is applicable to the bacilli of anthrax, symptomatic anthrax, diphtheria, leprosy, malignant œdema, mouse septicæmia, rouget, tetanus, tuberculosis, the Fraenkel diplococcus, micrococcus tetragenus, the various staphylococci and streptococci, actinomyces, moulds, and yeasts. It is not given by the bacillus of glanders, typhoid fever, hog cholera, Asiatic cholera, chicken cholera, influenza, plague, Friedländer's bacillus, colon bacillus, gonococcus, rhinoscleroma, and recurrent fever spirillum.

The Staining of Flagella.—Special care must be given to the preparation of the cover glass. The cultures should be made on freshly inclined, moist agar, and should, as a rule, be less than twenty-four hours old. A very dilute suspension of the growth is made, and when spread over the cover glass is allowed to dry in the air. The fixation must be done with the least amount of heat possible. This can best be done by passing the cover glass, held between the thumb and forefinger, through the flame.

In Löffler's method the specimen is covered with a mordant solution which consists of 100 parts of a twenty-per-cent. tannic-acid solution, 50 parts of a cold saturated ferrous sulphate solution, and 10 parts of alcoholic fuchsin. The cover-glass is heated over the flame so that vapors are given off for a minute or two. Every trace of the mordant must then be removed by washing with water, and if it has dried down around the edge, it should be removed with a knife. The last traces of the mordant can be removed by momentary immersion in absolute alcohol. The specimen is then heated with aniline water fuchsin for a couple of minutes, washed with water, and examined. The chief difficulty in this method lies in the formation of a heavy deposit of foreign matter, which masks the bacteria.

Fischer's mordant is a slight modification of that of Löffler. It consists of 2 gm. of dry tannin, 20 c.c. of water, 4 c.c. of ferrous sulphate (1:2), and 1 c.c. of concentrated alcoholic fuchsin. The aniline water fuchsin is made by adding about 5 gm. of fuchsin, and 1 c.c. of a one-per-cent. solution of sodium hydrate to 100 c.c. of aniline water.

Bunge employed a mordant consisting of 75 parts of concentrated tannin solution, 25 parts of a five-per-cent. solution of ferric chloride, and 10 parts of a concentrated aqueous fuchsin solution. After standing some days hydrogen peroxide is added until a reddish-brown color is obtained.

Pitfield makes use of a single solution of mordant and dye. Two solutions are first prepared: (1) consisting of 1 c.c. of saturated alcoholic gentian violet and 10 c.c. of saturated aqueous alum; (2) consisting of 1 gm. of tan-

nic acid and 10 c.c. of distilled water. The two solutions are filtered and then combined. The mixture is heated on the cover glass over a flame for about a minute, and then washed off.

Van Ermengem's method is essentially different. The cover glass is warmed for about five minutes with a fixing solution consisting of 60 c.c. of a twenty per cent. tannin solution, 30 c.c. of two-per cent. osmic acid solution, and four to five drops of glacial acetic acid. It is then washed with water, rinsed in alcohol, and dipped for one or two seconds in a sensitizing solution of silver nitrate (one-half to one per cent.). After this it is placed for a few seconds in the reducing solution which consists of 5 parts of gallic acid, 3 parts of tannic acid, 10 parts of sodium acetate, and 350 parts of distilled water. It is again placed in the silver nitrate solution, in which it is moved about until the liquid darkens, after which the preparation is washed with water, dried, and examined.

Of the numerous other modifications which have been proposed that of Gemelli only need be given. Gemelli cleans the cover glasses in a boiling mixture of potassium bichromate (three per cent.), and sulphuric acid (five per cent.). After washing in water they are kept in alcohol. Before use each cover glass is flamed several times. Gelatin cultures developed at 37° C. are said to give the best result. A loopful is transferred to 5 c.c. of water in a watch glass, and from this suspension a drop is taken and spread over a cover glass, which is then set aside over calcium chloride to dry. The specimen is then placed for ten to twenty minutes in a one-fourth-per-cent. solution of potassium permanganate. The preparation is now washed well in distilled water, after which it is placed in a three-fourths-per-cent. solution of calcium chloride (?), to which has been added a one-per-cent. solution of Grübler's neutral red in the proportion of twenty to one. After remaining in this for fifteen to thirty minutes the specimen is washed, dried, and mounted. The method is said to give excellent and sure results without the annoying precipitates which form in the other procedures.

Staining of Capsules.—Welch's method consists in treating the cover glass with glacial acetic acid for a few seconds. The excess of acid is drained off with a filter paper, after which the specimen is washed in aniline water gentian violet, and finally in a sodium chloride solution (0.85 to 2 per cent.). The heavily stained bacillus will be found to be surrounded by a pale violet halo.

Nicolle treats the cover glass with a mixture of one per cent. carbolic acid (100 parts) and concentrated glacial alcoholic gentian violet (10 parts). It is then washed in absolute alcohol containing one-third its volume of acetone, rinsed in water, dried and mounted.

Staining of the Babes-Ernst Granules.—Neisser recommends the following method as a means of differentiating the diphtheria bacillus from like organisms. A culture grown on Löffler's serum should be used. The specimen is treated for one to three seconds, or a little longer, with the following solution: 1 gm. of methylene blue, 20 c.c. of absolute alcohol, 50 c.c. of glacial acetic acid made up to one litre with distilled water. It is then washed with water and stained with Bismarck brown (two per cent. aqueous solution) for three to five seconds. Finally it is washed with water and examined. The blue granules will stand out in the light brown bacilli.

Piorkowski heats the preparation for one-half to one minute with an alkaline solution of methylene blue, then decolors for five seconds in alcohol containing three per cent. of hydrochloric acid. A one-per-cent. aqueous eosin is applied for contrast, after which the preparation is washed and examined.

Romanowsky's Chromatin Stain.—This method is extremely valuable for staining protozoal parasites, such as those of malaria and the trypanosomes. When properly carried out it gives an admirable differentiation of the chromatin, which appears red on a blue background. Nocht's modification gives very good results, and is briefly as follows: A solution of one-per-cent. methylene blue and one-half per cent. of sodium carbonate is kept at about 60° C. for several days to "ripen." The change which takes place is one of slow oxidation, and as a result a number of products form, among which is the one which is essential to this method. This active red constituent has been designated as methylene azur. To about 2 c.c. of water in a watch glass two to three drops of a one-per-cent. solution of eosin are added, and then the altered blue, drop by drop, till the eosin tint just disappears. The specimen is floated on this dye for five to ten minutes, after which it is washed and examined.

Independently Wright, Leishman, and Reuter arrived at a simple modification. The ripened or polychrome methylene blue is treated with an eosin solution to slight excess. The precipitate, which Reuter has called a methylene-blue eosin, is then filtered, washed and dissolved in methyl alcohol. This solution can now be obtained from Grübler. Thirty drops of this are added to 20 c.c. of distilled water in a large watch glass or Petri dish. The specimen, which can be fixed with ether alcohol or with formaldehyde alcohol (10:90), is immersed in the dye for fifteen to thirty minutes. It is well gently to agitate the liquid from time to time. It is then washed, dried, and mounted.

Giemsa prepares the stain by adding 1 c.c. of a 0.08-per-cent. solution of methylene azur hydrochloride, Höchst, to 10 c.c. of a 0.005-per-cent. aqueous solution of Höchst eosin. Laveran employs 1 c.c. of a one-per-cent. solution of azur, 2 c.c. of a 0.1-per-cent. solution of eosin, and 8 c.c. of water. The specimen is stained for ten minutes, then washed and immersed for two to three minutes in a five per-cent. tannic solution, after which it is washed, dried, and mounted.

Impression Preparations of Colonies.—It is very often desirable to reproduce or preserve the characteristic surface colonies. The selection of the surface colony is made under the microscope, after which the tube of the instrument is raised and a cover glass is dropped down upon the colony. Gentle pressure is applied, the cover glass lifted off, air-dried, fixed, and stained with methylene blue in the usual way.

Staining of Sections.—In order to study the finer distribution of bacteria in the body of an infected animal it is necessary to harden portions of the different tissues and organs, which are then cut up into sections. The tissue may be cut by the aid of a freezing microtome, but the best results are obtained when the material is embedded in celloidin or in paraffin. The latter is especially to be recommended. The methods which are used for this work are essentially histological, and need not be considered in this connection.

To obtain a simple stain the section is placed in the dilute aniline dye for about five minutes. Dilute carbolic fuchsin or carbolic methylene blue are very good for this purpose. It is then washed thoroughly in water and transferred to very dilute acetic acid (1 c.c. of glacial acetic acid to 1,000 c.c. of water). The section is now placed in strong alcohol for one-half to one minute to remove the excess of dye. After washing in water it may be examined, and if the decoloration has not been sufficient, the treatment with alcohol can be repeated. When properly differentiated the section is placed for a few seconds in absolute alcohol for dehydration, then cleared in oil of cloves, passed through xylol and mounted in Canada balsam.

In Kühne's method the sections are stained in carbolic methylene blue and differentiated in one-half per cent. hydrochloric acid, rinsed in dilute lithium carbonate solution, then in water. The section is transferred to absolute alcohol, which is slightly colored with methylene blue for one-half minute; then for a few minutes to aniline oil containing methylene blue, finally into clear aniline oil, turpentine, xylol, and balsam.

Nicolle stains the sections in carbolic thionin, washes in water for about a minute, dehydrates with absolute alcohol, clears up in oil of cloves, and mounts in balsam. Another procedure employed by him is to stain first with Löffler's methylene blue, differentiate in one-half per cent. acetic acid, and fix in ten-per-cent. solution of tan-

nin for a few seconds. The section is then washed, dehydrated, cleared, and mounted.

Gram's stain is applied to sections in the following manner: The section is placed in the freshly prepared aniline water gentian violet for about ten to fifteen minutes, after which it is washed in water, or better in aniline water, to remove the excess of dye. The section is then placed in Lugol's iodine for three to five minutes, transferred to absolute alcohol, in which it is tilted about until the excess of the stain has been removed and only a pale violet color remains. Ebner's solution may also be used for decoloring. It is counterstained in very dilute eosin for about a minute, washed in water, dehydrated in absolute alcohol, cleared in cloves, and mounted.

Bismarck brown may be used for a contrast color, or Weigert's picrocarmine. The latter may be made by adding 1 part each of carmine and ammonia to 50 parts of water; to this solution picric acid is added until a precipitate forms which is dissolved by the addition of a little ammonia; finally a few drops of carbolic acid are added.

Tubercle and leprosy bacilli can be stained in sections by applying the principle employed for cover-glass preparations. The carbolic fuchsin should be warmed to about 40° C. in a Petri dish. The sections remain in this solution for fifteen to thirty minutes, after which they are washed in water to remove the excess of dye. They are then decolored in dilute acid, or better in Ebner's solution. The latter consists of one-half part each of sodium chloride and hydrochloric acid, 30 parts of water, and 100 parts of alcohol. The faint pink sections are then placed in Löffler's methylene blue solution for about half a minute, after which they are dehydrated in absolute alcohol for a few seconds, transferred to xylol, and mounted in balsam.

Diagnostic Methods.—The general principles which have been given find their practical application in the diagnosis of disease. It is desirable, therefore, to indicate briefly the way in which these methods are applied.

1. *Actinomycosis.*—The pus should be examined unstained under a cover glass for the characteristic yellowish, radiating masses with club-shaped threads along the border. Permanent preparations may be made by making smears, and staining either by the simple or by the Gram method. The pus may be hardened in mercuric chloride, sectioned and stained by Gram. Curettings may be treated in like manner.

2. *Anthrax.*—Cover-glass smears of the blood are stained by the simple and by the Gram method. Confirmation of the nature of the organism found can be obtained by inoculating a white mouse or a guinea pig subcutaneously with the material. This with the cultural characteristics will enable identification.

3. *Bubonic Plague.*—This diagnosis may be made during life, but more often after death. In the pneumonic form the blood-streaked sputum can be used for simple stains, which will show large numbers of the small rods. In the bubonic type the enlarged gland may be punctured and thus material obtained for examination. The detection of the bacillus in the blood can be effected by drawing several cubic centimetres of the blood from a vein by means of a syringe. Agar plates, one part of blood to two parts of agar, should then be made. Whether the result is apparently positive or wholly negative, an animal experiment must be carried out. The suspected material is inoculated subcutaneously into a guinea-pig, and if plague bacilli are present, death will ensue in from five to eight days. Cultures and smears from the animal will then establish the nature of the organism. An important cultural characteristic is brought out by planting the material on agar containing about three per cent. of salt. Round or pear-shaped involution forms develop. The smears from the body should be stained with Löffler's methylene blue or with carbolic thionin. The short rods take the bipolar stain, and if the material is old, roundish involution forms or "doughnuts" will be met with. The bacilli are not stained by Gram.

4. *Cholera.*—The examination may aim to find the cholera vibrio in the drinking-water, or it may be concerned with the diagnosis of the disease. In the latter case the rice-water discharges should be collected and searched for mucous flakes. Preparations from these, when stained, will show the presence of the characteristic vibrio. The appearance of the colonies on gelatin and on agar plates, the growth in bouillon, and the indol reaction serve to identify the organism. The intraperitoneal injection of the culture into a guinea-pig should also be practised. The most important reaction is that of Pfeiffer. It consists in injecting into the peritoneal cavity of a guinea-pig a mixture of the cholera antiserum and the suspected organism. Every few minutes a drop of fluid is withdrawn from the peritoneal cavity by means of a capillary tube and examined. If the organisms persist, it is safe to say that they are not those of true cholera. The latter under these conditions lose motion, become granular, and soon disappear.

It may be possible under exceptional circumstances to detect the cholera vibrio in drinking-water by ordinary plating on gelatin. Obviously the number of the organisms may be so small and the other bacteria may be so numerous that it is impossible to obtain positive results by this method. To overcome this difficulty Schottelius devised his enriching method. This consists in adding the suspected water to a one-per-cent. solution of peptone and incubating at 37° C. for about twelve hours. The actively motile cholera spirilla, on account of their need of oxygen, accumulate as a cloudy layer near the surface. A loop of this liquid is then transferred to and spread over the surface of gelatin and agar plates, and the further identification is then easily effected. Obviously the peptone may be added direct to the water, for example 100 c.c., and in this way the presence of a very few vibrios in a large volume of water may be detected.

5. *Diphtheria.*—The necessary material for the examination is obtained either by means of a Roux spatula (Fig. 5083), or by a cotton swab. The cotton swab is usually employed, and is made by twisting a piece of cotton about the end of a thick iron wire. The wire should be about six inches long. The cotton end is then placed in a plugged test tube which is sterilized by dry heat. Whether a pseudo-membrane is present or not, scrapings are made from the surface of the affected tonsils or throat and examined. Usually the swab is streaked over the surface of one or more tubes of plain, or better Löffler's serum. These tubes are incubated overnight and examined in the morning for the characteristic diphtheria bacilli. The cover-glass preparations made from these cultures are stained with Löffler's methylene blue. The swollen rods with irregularly stained contents are easily identified. In case there is any doubt as to the diagnosis, it is advisable to inoculate a guinea-pig with the culture material.

Whenever possible it is advisable to make cover-glass preparations direct from the false membrane. These are then stained with Löffler's methylene blue. The diagnosis can be made thus often in a few minutes.

6. *Dysentery.*—It is necessary to distinguish between two types, the bacillary and the amœbic. The examination for amœbæ should be made at once, immediately after the stool is passed, in order to obtain actively motile organisms. A drop of the thin fæces or suspension is placed on a slide, covered with a cover glass, and examined under the microscope. The characteristic motion will leave no doubt as to the nature of the organism. The motion can be observed best on a warm side or in an incubator. Staining is not necessary.

The bacillary form is due to the bacillus dysenteriæ, and the diagnosis of this type necessitates the detection of this organism. Agar plates should be made from the stools and developed at 37° C. From the suspected colonies subcultures should be made to glucose agar, lactose litmus agar, and mannite litmus agar. The pure cultures should finally be tested for agglutination with the serum of a dysenteric patient. Too much care, however, cannot be exercised in drawing conclusions based upon a

positive agglutination reaction, since this test is undoubtedly given by allied organisms.

7. *Gonorrhœa.*—Cover glass preparations made from the pus will serve to establish the diagnosis in nearly all instances. They should be stained with Löffler's methylene blue. A fair double stain can be obtained by first applying eosin, after which the blue can be used for a few seconds. The result is a more or less pink background with blue gonococci. Gram's method is negative.

Von Wahl recommends the following method of double staining which brings out the gonococci as reddish-violet to black cells on a light green background. The stain consists of: Concentrated alcoholic solution of auramin, 2 c.c.; ninety-five-per-cent. alcohol, 1.5 c.c.; concentrated alcoholic solution of thionin, 2 c.c.; concentrated aqueous methyl green, 3 c.c.; water, 6 c.c. The auramin and thionin solutions are prepared by dissolving the dyes in hot ninety-five-per-cent. alcohol to saturation, cooling, and filtering. The cover glasses are stained for five to fifteen seconds. The ordinary bacteria stain feebly or not at all.

The detection of the gonococcus in septicæmic cases can be accomplished by drawing 5-10 c.c. of blood from the vein of the arm and adding this, in about equal parts, to melted agar at 45°. The mixture is at once poured into Petri dishes, and these are developed at 37° C. In this way the gonococcus can be detected when direct stains would fail to show the organism.

The culture test for the gonococcus is rarely resorted to on account of the difficulty of obtaining the necessary blood or serous fluids. The ordinary media have always been regarded as unfavorable for the growth of this organism. According to Thalmann, Wildbolz, and others, the gonococcus can be grown on ordinary one-and-one-half-per-cent. meat peptone agar. Thalmann recommends very highly such a medium for diagnostic purposes, and especially where direct microscopic examination is unsatisfactory or negative. The acidity of ordinary agar or bouillon is reduced by the addition of two-thirds of the amount of alkali necessary to make the media neutral to phenolphthalein. The preparation of these media has been given.

8. *Leprosy.*—The leprous nodules are characterized by the presence of enormous numbers of the specific bacillus which can be readily detected by staining. The Ziehl-Neelsen method, as employed for the tubercle bacillus, will give excellent results if the tissue is reasonably fresh. When kept for some time in alcohol the bacilli lose their staining properties so far as this method is concerned, but they can still be found by means of Gram's method. Animal inoculations and cultures are not possible.

9. *Meningitis, Cerebro-spinal.*—The diplococcus intracellularis meningitidis is found in the cerebro-spinal fluid. Hence during life it is necessary to remove some of the fluid by lumbar puncture. This fluid should be planted abundantly on glycerin, or better on serum agar. Cover-glass preparations made direct will show the typical organism resembling the gonococcus in form and in its presence within the leucocytes. It is not stained by Gram's method, but can be given a double stain by that of Pick and Jacobsohn, or by the modification suggested by Fraenkel. The dye is made by adding to 20 c.c. of water eight drops of a saturated solution of methylene blue, and then forty to fifty drops of carbolic fuchsin. The dye is allowed to act for five minutes. The cocci are blue on a red background.

10. *Pneumonia.*—In all pneumonic conditions the blood-streaked sputum should be examined by making simple and Gram stains. In this way it becomes possible to recognize the pneumonic form of plague. Ordinarily, however, pneumonia is due to the Fraenkel diplococcus and at times to the Friedländer pneumobacillus. The form, staining and cultural properties of these organisms permit ready differentiation and identification. The lance-shaped diplococcus of Fraenkel, as found in the body, is surrounded by a capsule, and is stained by Gram's method. The colonies and cultures on glycerin agar are very faint and dewdrop-like, and tend to die out in a few days. Their vitality and virulence are best preserved by cultivating them on rabbit blood or serum agar. In doubtful cases the material should be injected under the skin of the ear of a rabbit. If death results the diplococcus will be found in large numbers in the heart blood and organs of the animal.

11. *Rabies.*—The cause of this disease is as yet unknown, but it is to be found, in pure condition so to speak, in the brain and spinal cord of the affected person or animal. The diagnosis rests upon animal inoculation with such material. A few drops of a suspension of the brain or cord are injected subdurally into a rabbit or guinea-pig. The method has been already described.

The histological changes in the nervous system are very slight, and it has been suggested that the diagnosis of rabies may be hastened by making an examination of sections of the cord and ganglia. The lesions are not sufficiently marked in all cases to permit diagnosis, and for that reason this method should not be relied upon to the exclusion of the only positive test, that of animal inoculation.

12. *Tetanus.*—The point of inoculation must be found first. This may not always be easy, for the original wound may have healed over. The portal of entry may be a bad tooth, or the wound produced by an old rusty nail, a splinter of wood, or the powder grains of a pistol. Cover-glass preparations should be made from the pus, if there is any; and, if not, from such serum, blood or tissue as can be obtained from the wound. They should be stained with carbolic fuchsin. The specimen should be examined for "drum sticks" or rods with terminal spores, and particularly for the presence of rather narrow, long bacilli. These are present even when no spores can be found.

Cultures should be made on glucose litmus gelatin, and at the same time a series of glucose agar plates should be made and developed at 37° C., either in hydrogen or in the pyrogallate apparatus. The original tissue should be planted under the skin of a white mouse and of a guinea-pig. The cultures when developed are carefully searched for the drum-stick forms.

13. *Tuberculosis.*—The pulmonary form is usually recognized by an examination of the sputum, preferably that which has been collected in the morning on rising. The cheesy particles, if such can be recognized, should be picked out by means of the wire and spread over the cover glass. The specimen is then stained by the Ziehl-Neelsen method already given. The red rods on a blue background are readily recognized.

The same method is employed in the examination of pleuritic fluid, pus, urine, milk, etc. In all these examinations, however, two facts should be borne in mind. In the first place the tubercle bacilli may be present, but in such small numbers that they escape detection. Again, acid-resisting organisms, such as the leprosy, smegma, timothy grass bacillus, etc., may be present, and may be easily mistaken for the tubercle bacillus.

In either case it is the animal experiment which will serve to remove the doubt. When the tubercle bacilli are few or doubtful, it is well to submit the material to preliminary centrifugation. The deposit can be used then for staining and for injection. The injections should be made into the peritoneal cavity of the guinea-pig. If tubercle bacilli are present in the material used, even if so scarce as to be unrecognized by the microscope, the animal will develop the disease and will die in the course of a month or two. The tuberculous organs and glands can be examined then for tubercle bacilli, and cultures can be made on glycerin agar, potatoes, and on Hesse's Heyden agar. The acid-resisting bacilli, other than the tubercle bacillus, are not fatal to animals, and, moreover, the histological changes which they induce are quite different from those caused by the tubercle bacillus.

14. *Typhoid Fever.*—The verification of the diagnosis is usually made by means of the agglutination test of Widal, which will be described later. The direct detection of the typhoid bacillus in fæces, urine, blood, rose spots, and in water presents marked difficulties. The

reason for this lies in the very great similarity which exists between the typhoid and the colon bacillus. Numerous methods have been devised for the purpose of effecting a distinction between these two organisms; and while it is an easy matter to differentiate between the pure cultures of the typical organisms it becomes vastly more difficult under natural conditions, especially when, as often is the case, the para-colon and para-typhoid bacilli are present.

Some of these methods endeavor to restrict the growth of the colon and of adventitious bacteria by the addition of antiseptic substances to the media. Thus carbolic bouillon, Parietti's carbolic hydrochloric-acid broth, and crystal violet are used with this object in view, but there can be no doubt that weak typhoid bacilli are also inhibited.

Other methods are based upon the unequal diffusion of the two organisms in special media. The Stoddart, Hiss, and Capaldi media belong to this class. Again, the effort is made to bring out differences between the colonies of the Eberth and colon bacilli, as in the case of the Holz potato gelatin, Elsner, Weil, Hiss, and Piorkowski media. These are all described in the foregoing pages. Still other methods seek to utilize the differences in the fermentative powers of these organisms, as evidenced in the production of gas, acid products, etc. Lastly, there are several methods which have only recently been devised in which the distinction is effected by means of the agglutination reaction. That of Windelbandt, as modified by Schepilewsky, certainly seems to be effective in detecting typhoid bacilli in tap water. Its real value in the examination of typhoid fæces remains to be demonstrated.

Schepilewsky's procedure is as follows: Several cubic centimetres of the infected water are added to 50 c.c. of bouillon in an Erlenmeyer flask, which is then incubated for twenty-four hours at 37° C. The culture is now filtered through a sterile cotton filter in order to remove any compact masses of bacteria which may be present. The filtrate is received in conical centrifugating tubes. A very active serum from a rabbit, which has been immunized to the typhoid bacillus, is then added to the cloudy filtrate, and this is set aside for two to three hours at 37° C. If many typhoid bacilli are present, visible agglutination may be noted; but if they are not abundant, the masses will be so small that agglutination may not be detected. In either case the tubes are centrifugated for one to two minutes, after which the fluid is decanted and the tubes are inverted so as to drain as completely as posssible. Sterile sodium chloride solution is then added to the tubes and the deposit is taken up and transferred to a sterile test tube which contains glass beads. By vigorous shaking the agglutinated masses can now be broken up and homogeneous suspension obtained. A glass rod, bent at right angles, is then dipped in the suspension, and streaked thoroughly over the surfaces of a number of plates of the special agar. The latter is a three-per-cent. agar, to which after sterilization in an autoclave a lactose and lacmoid solution is added. This consists of 1.5 per cent. lactose and 0.04 per cent. lacmoid, and before addition is boiled fifteen minutes. The Petri dishes are developed at 37° C. for twenty-four hours. The typhoid colonies are round, or oval, and sharp bordered; later they show the typical spreading form, and the color of the centre changes to a dirty yellow.

The typhoid-like colonies should then be examined under the microscope and submitted to further identification. A suspension of the colony may be tested for the agglutination reaction with typhoid serum. Pfeiffer's reaction may be tested for by injecting a mixture of antityphoid serum and the organism into the peritoneal cavity of a guinea-pig, as described under Cholera. The cultures should also be tested for gas production, indol, milk coagulation, and on the special plating media.

In the absence of the serum necessary for the above method recourse may be had to the plating medium of Hiss, the urine gelatin of Piorkowski, and the Drigalski-Conradi agar, the preparation of which has been given.

15. A number of infections due to moulds and allied forms and also to yeast-like bodies have been described. The former are represented by the streptothrices, or, more correctly, by the actinomyces of Madura foot and of cattle farcy. The yeast or blastomycotic affections have been noted in certain forms of dermatitis, and may even be systemic in character. In all these diseases the examination of the pus and of sections of tissue, as well as the culture of the organism, must be carried out.

16. *Protozoal Diseases.*—Several very important diseases are due to organisms of this class. The examination for amœbæ in tropical dysentery has already been touched upon. The sporozoa include among others the plasmodium of malaria, the piroplasma of Texas fever,

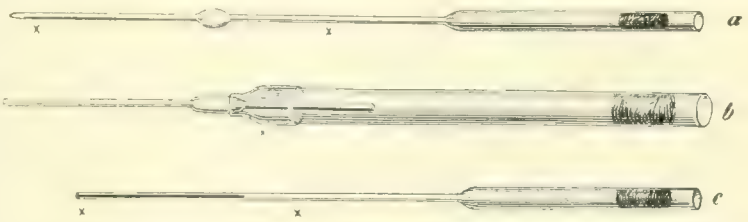


FIG. 5109.- Filling of Capillary Tubes for Thermal Death-point Determinations. *a*, Tube filled ready to be sealed at *x x*; *b*, emptying of tube. (Novy.)

of "spotted fever," and of horses, sheep, and dogs. The flagellata cause the various trypanosomatic diseases, such as the surra of Asia and of the Philippine Islands, nagana or the tsetse-fly disease of South Africa, dourine or "maladie du coït" of the Mediterranean littoral, caderas of South America, the gambian fever and the sleeping-sickness, the last two being diseases of man. Moreover, many animals harbor in the blood parasites of this group, as in the case of the wild rat.

In all suspicious cases the blood should be examined for these two groups of organisms. The plasmodium of malaria is found especially within the blood cells. The trypanosomes are free in the plasma. The blood may be examined direct under the cover glass, or in hanging drop, or in a Ranvier slide. Stained preparations can be made with methylene blue, thionin, or best with some modification of the Romanowski method. The preparation of the specimens and the staining methods have already been described. The trypanosomes of the Nile and of nagana, cultivated by Novy and McNeal, are the only pathogenic protozoa which it has been possible to grow artificially. Their presence is best detected by direct examination of the blood, though at times they may be very difficult to find, and may require daily examinations for several weeks.

DETERMINATION OF THE THERMAL DEATH POINT OF BACTERIA.—In this work and also in testing disinfectants it is necessary to have almost homogeneous suspensions of the organism to be tested. Water suspensions should be used first, and later those of bouillon, serum, etc. The liquid is introduced by means of a bulb pipette into the tube of an agar culture. The growth is rubbed up as much as possible, and the suspension is then transferred to a sterile glass-wool filter. In this way the masses of bacteria are removed. The cloudy filtrate may be used as such, or it may be diluted so as to have fewer organisms in the test. It may be used as such for determining the action of moist heat and for testing disinfectants. Again, for dry-heat work and for many disinfecting tests the suspension is allowed to dry upon the surface of sterile glass slips, glass or garnet beads, silk threads, muslin squares, etc.

To test the action of dry heat a number of cover glasses on which the test organism has been dried are placed in a sterile Petri dish and exposed to a given temperature.

At given intervals a specimen is removed and planted in bouillon.

To test the action of moist heat the best procedure is to draw up the liquid into sterile capillaries, as shown in Fig. 5109. The tube is sealed, below and above, the liquid. The advantage of this method lies in the fact that the heat promptly penetrates every part of the suspension. A number of tubes thus equipped are placed in a water-bath, the temperature of which is kept at a constant point by means of a regulator. At intervals a capillary is removed, cooled, opened at one end, and the contents are expelled into a tube of bouillon by gently touching the closed end to a flame.

Testing of Chemicals.—In this work it is necessary to distinguish between the antiseptic and the disinfecting action of a substance. The former refers to the amount of the substance which will inhibit the growth, but not necessarily kill the organisms. The latter implies the actual destruction of the test object. Obviously a substance which will kill bacteria, when diluted sufficiently will merely restrict their growth; and when the dilution is excessive will have no action whatever.

The antiseptic action is determined by adding to the suspension in bouillon varying amounts of the chemical so as to make different dilutions, for example: 1 in 500, 1 in 1,000, 1 in 5,000, 1 in 10,000, etc., solutions. The tubes thus equipped are then placed in the incubator for several days. The very weak solutions will show growths, while the very concentrated ones will show none. The amount which just inhibits the growth represents the antiseptic power of the substance.

The germicidal action of a gas, such as formaldehyde, is determined by exposing cover-glass preparations, silk threads, bit of muslin, etc., impregnated with the suspension, dry and moist, to the action of the gas in a tight room. At the end of the exposure the preparations are transferred to sterile tubes of bouillon and incubated.

The germicidal action of liquids is ascertained, either by adding the solution to the bacterial suspension or by immersing in the solution the dried cover-slip preparations mentioned. In the former case, at stated intervals, a small loop of the liquid is transferred to bouillon, while in the latter case the slip or thread is first rinsed in sterile water and then placed in the bouillon.

The Serum Agglutination Test.—The serum of an animal which has been immunized to a germ when brought into contact with a suspension of that germ will cause the organisms to gather in masses. This fact is utilized in the Widal test for typhoid fever. A drop of the serum from a typhoid patient is diluted with ten, twenty, thirty, fifty, one hundred drops respectively of water in a watch glass. A drop of each mixture is then transferred to a cover glass and inoculated with a very small amount of a fresh agar culture of the typhoid bacillus, care being taken to avoid an excess of the organisms. Hanging drops are then made and the preparations examined under the microscope. The limit of the reaction is indicated by the dilution which is just able to cause paralysis of motion and clumping in one hour. Instead of diluting with water some prefer to use a very young bouillon culture. The agglutination test is most delicate when carried out under the microscope. Very good results, visible to the unaided eye, may be obtained by adding the serum to bouillon cultures of the organism. The tubes thus treated should be set aside for some hours at 37° C. when the agglutinated masses will settle to the bottom and leave the liquid clear. When applying the test to a suspected case of typhoid fever it is not always possible to obtain large amounts of the serum. In such instances the blood may be placed in single drops on a sheet of filter paper, or better tinfoil. The dilutions can then be made with these drops of dried blood as with the serum itself. The application of this test to the recognition to the typhoid bacillus in drinking-water, fæces, etc., has been given.

Testing the Strength of Antitoxin.—The strength of an antitoxin is expressed in immunity units. A unit represents that amount of serum which will be just sufficient to save a 250-gm. guinea-pig against 100 minimum fatal doses of the diphtheria toxin. Thus if 0.1 c.c. of serum protects against this dose of poison, then it will contain 1 immunity unit, and 1 c.c. of such serum will contain 10 immunity units. It is possible to prepare diphtheria antitoxin of such strength that 1 c.c. will contain more than 1,000 immunity units. Usually, however, the serum as marketed contains about 200 immunity units per cubic centimetre.

The first essential is to ascertain the minimum fatal dose of the toxin, by which is meant the amount of toxin which will kill a 250-gm. guinea-pig on the fourth, or at most on the fifth day. The toxin itself is a bouillon culture of the diphtheria bacillus, which has been rendered sterile by the addition of a small amount of carbolic acid. The diphtheria culture should not be more than a week old.

Varying amounts of the serum are then added to portions of the toxin representing one hundred minimum fatal doses. These mixtures are then injected into guinea-pigs of the weight given. That fraction of a cubic centimetre of the serum which just suffices to save a guinea-pig under these conditions represents, as stated above, one immunity unit. The test is usually made with only ten minimum fatal doses, in which case the proper correction is made.

This method is subject to some error, inasmuch as it has been found that a serum which has been tested against one toxin will show a different value when tested against another. This is due to the fact that the toxin undergoes changes on keeping, and is converted into a non-poisonous body or toxoid, which, however, retains the power of combining with the antitoxin. For this reason Ehrlich proposed a new method of testing the antitoxic value of a serum. A standard dried antitoxin is made the basis of the measurement. This is diluted so that a given amount just represents one immunity unit. The test dose of toxin is then ascertained and represents the amount of toxin, which mixed with one immunity unit of serum, will cause death on about the fourth day. The serum to be tested is then diluted, mixed with the test dose of the toxin, and injected into guinea-pigs. If the animal dies in a day or two it is evident that the serum contains less than one immunity unit. If, on the other hand, it lives for seven or eight days, or even recovers, it shows that the amount of serum taken contains more than one unit. By using suitable dilutions of the serum eventually the point will be reached where the amount taken will represent exactly one unit.

Methods of Immunization.—Only the general principles of active immunization can be considered. The injections are made subcutaneously, intraperitoneally, and intravenously. When a soluble poison is injected, a true antitoxin develops in the animal and is present in the blood, and hence in the serum. This is the case in diphtheria, tetanus, and venom immunity. On the other hand, when the solid cell is injected, the serum may acquire anti-infectious properties, the best instance of which is seen in the anti-pest serum. The organisms may be killed by exposing them to the action of ether, chloroform, or to that of moist heat at 60° C. In special cases the attenuated living germ is used, and at times even the most virulent form is employed. By the injection of cells other than bacteria, diverse cytolytic sera are obtained. Thus the injection of the red blood cells gives rise to a hæmolytic serum. The temperature and the weight of the animal must be taken daily, since they afford the best indication of the condition of the animal.

Examination of Air.—The bacteria which chance to be present in the air are in a dried condition, and tend to settle when the motion of the air is lessened. The simplest method consists in exposing a plate of gelatin or agar to the air for a given length of time. Some of the organisms settle on the gelatin, and eventually give rise to colonies. Koch improved slightly upon this by placing the gelatin plate in the bottom of a sterile cylinder of known volume. After opening the cylinder in a given locality it is closed with a cotton plug and set aside, when

the organisms contained in that volume of confined air settle to the bottom on the surface of the plate. The results, it will be seen, are crudely quantitative (Fig. 5110).

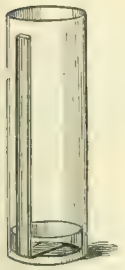


FIG. 5110. Koch's Cylinder for Air Analysis.

Hesse's method consists in drawing the air through a large Esmarch roll tube (Fig. 5111). The volume of the air drawn through can be determined from that of the aspirating bottles. The bacteria in the air impinge upon the gelatin surface where they develop into colonies which can be counted and studied.

The apparatus of Petri, although very expensive, may be said to give the best results. It consists in the first place of an air pump, which automatically registers the movement of the piston, and thus gives the volume of the air which has been drawn through. The air is aspirated through a tube (Fig. 5112) containing several layers of sterile sand. The suspended bacteria are thus held back. At the close of the operation

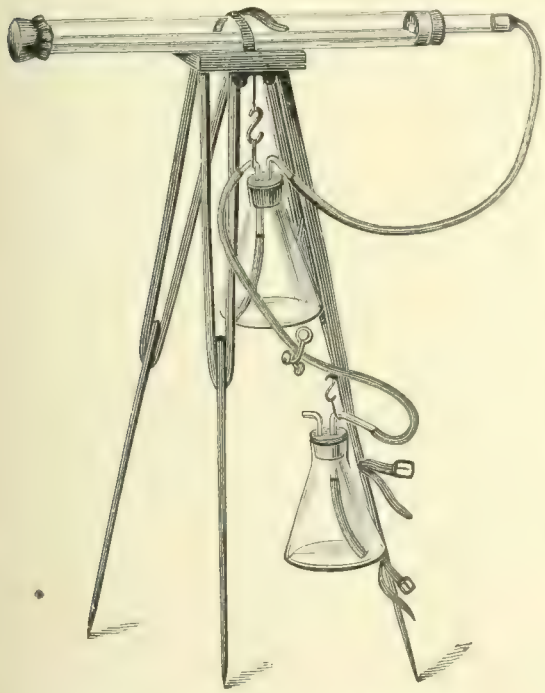


FIG. 5111. Hesse's Apparatus for Air Analysis.

the sand is transferred to a Petri plate, where the bacteria will form colonies and thus become accessible for study.

Instead of sand, Sedgwick and Tucker employed a filter of sugar. The special tube employed by them is shown in Fig. 5113. After the air has been drawn through, the sugar is tapped down into the wide portion of the tube, then gelatin is added and warmed until the sugar dissolves, after which an Esmarch roll culture is made in the same tube.

Other workers have filtered the air through liquid media or through gelatin. The most convenient form of apparatus of this kind is that of Wurtz, shown in Fig. 5114. A suitable amount of gelatin is placed in the sterile tube, then a known volume of air is drawn through, after which the gelatin is solidified over the inner wall of the tube, thus forming a roll culture.

Examination of Soil.—By means of a small sterile platinum spoon a definite volume of the soil may be transferred to a Petri plate, where it is thoroughly mixed with the medium. The colonies which develop can then be examined. In this way it is possible at times to demonstrate the presence of the anthrax bacillus in the soil of an infected locality. The detection of other pathogenic bacteria, as for instance those of tetanus and malignant œdema, can best be made by introducing a quantity of the soil under the skin of a guinea-pig or rabbit.

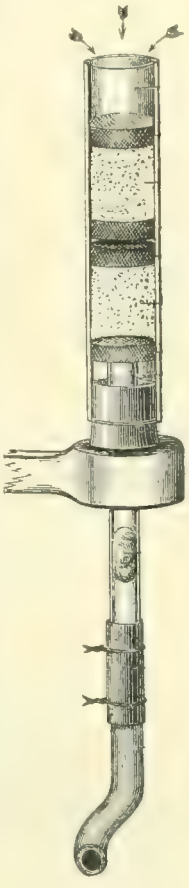


FIG. 5112.—Petri's Sand Filter for Air Analysis.

Examination of Water.—This is a very important procedure, and an enormous amount of work has been done to perfect the methods of work. The method followed will necessarily depend upon the immediate object in view. Thus the detection of the cholera vibrio is carried out in a different way from that used for the colon bacillus. The isolation of the cholera and typhoid organisms from water has already been described.

The water which is to be tested bacteriologically must be received into a sterile glass-stoppered bottle, and should be examined at once. The first step in the examination is to make gelatin plates. By means of a sterile pipette 1 c.c. of water is added to a tube of gelatin, mixed thoroughly, and the gelatin is then poured out into a Petri plate. In the same way plates are made with 0.5 c.c. and with one drop of the water. The gelatin plates are developed at 20° C. for several days. The colonies are then counted and examined in the usual way. When only a few colonies are present on a plate they can be readily counted with the eye. When the number is large special counters are made use of. That of Wolffhügel (Fig. 5115) is ruled in squares of 1 cm. and fractions thereof. Another form is that of Lafar. A very useful and cheap substitute is made by printing the divided circle on card paper. To make a count, the number of colonies in ten or more squares are ascertained and the average per square centimetre is obtained. The area of the gelatin on the plate is taken and then the total number of colonies on the plate determined, and the result is expressed per cubic centimetre of water.

Instead of using Petri plates, the Esmarch roll tube can be made. To count the colonies in such a tube Esmarch devised the counter shown in Fig. 5116.

When the number of colonies is likely to be extremely numerous, as in the examination of polluted water, it is advisable to dilute a portion of the sample with a known volume of sterile water. If the colonies are very nu-

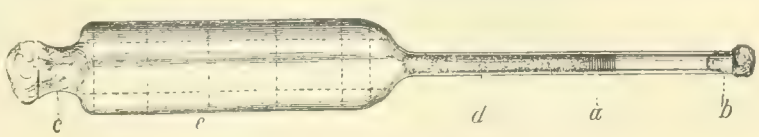


FIG. 5113.—Sedgwick and Tucker's Aërobioscope.

merous on a plate the counting can be carried out best under a microscope. Ehrlich stops are placed in the eye-piece or the special Ehrlich ocular may be used. The size of the opening in the ocular must be determined by means of a stage micrometer. The average number of colonies for a given sized opening is determined, and from this the total number on the plate is calculated.

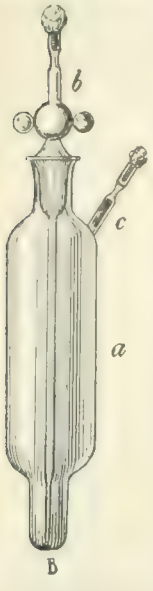


FIG. 5114.—Wurtz's Apparatus for Air Analysis.

The above method of examination gives approximately the number of bacteria which are present in a water, and to some extent information as to the kind of bacteria. It is of great value, therefore, in controlling the work done by the water filters. In order to ascertain the presence of pathogenic and other bacteria special methods must be resorted to. The method which has been employed during the past fifteen years in the Hygienic Laboratory of the University of Michigan consists in planting a cubic centimetre and a drop of the water in tubes of bouillon, which are then incubated at 39° C. If no growth forms, as often is the case, pathogenic bacteria may be said to be excluded. When a growth does form, a portion (1 c.c.) is injected into a guinea-pig. In case the animal dies the heart blood is examined for the kind of organism present. If no ill effects follow the injection, the water may be said to be free from pathogenic bacteria.

Sewage contamination is usually indicated by the presence of colon bacilli and of streptococci. The presence of the former is tested for by means of the Smith fermentation tube (Fig. 5117); 1 c.c. of the water is added to glucose bouillon in the fermentation tube, which is then set aside at 37° C. The formation of gas indicates the probable presence of the colon bacillus, while the non-production of gas points to the absence of this organism. Further tests are necessary for identification.

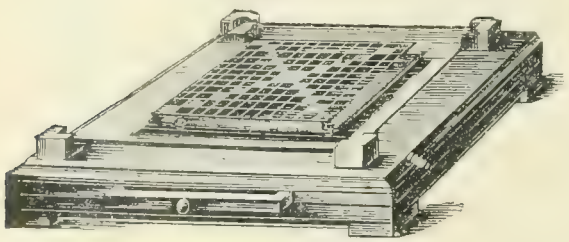


FIG. 5115.—Wolffhügel's Colony Counter.

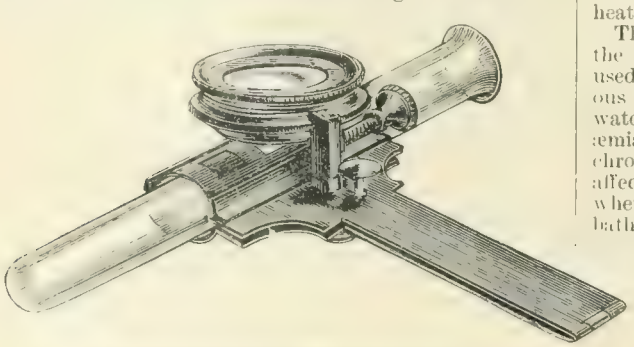


FIG. 5116.—Counter for Esmarch's Roll-Tube Cultures.

Litmus lactose agar plates should be made directly from the water and also from the fermentation tube when gas production is present. The formation of red colonies is indicative of the colon bacillus, since this organism ferments lactose, whereas typhoid-like bacteria do not. For the same purpose lactose bouillon is sometimes employed in the fermentation tube.

FIG. 5117.—Smith's Fermentation Tube.

Another procedure is to plant the water in carbolic bouillon, or in Parietti's solution, in order to eliminate many of the more common bacteria.

Neutral red bouillon and agar is also used for cultivating the suspected colon bacillus. The water may be planted direct, or the red colonies which form on the plate may be used for inoculation. The coagulation of milk and the production of the indol reaction are additional tests of identification. *F. G. Novy.*

BADEN-BADEN AND THE BLACK FOREST, GERMANY.—The region of the Black Forest (Schwarzwald) lying to the east of the Rhine, between Karlsruhe and Basel (Switzerland), is a thickly wooded mountain range of great beauty and picturesqueness, containing many climatic and mineral-water health resorts. The most of these resorts have only a summer season extending from about the middle of May to the end of September; but the open-air cures for pulmonary tuberculosis remain open the whole year, and the winter season is just as efficacious in the treatment of this disease as are the milder seasons of the year. The climate in general is that of Central Europe, with the addition of the peculiar influence of the mountains and the thick fir forests. The elevations of the climatic resorts are from one to two thousand feet. In this country comparable resorts are such places as Rutland, Mass., Saranac in the Adirondacks, and Liberty, N. Y.

Baden-Baden (650 feet) lies at the entrance of the Black Forest from the north, six miles from the Rhine, and is beautifully situated; it is surrounded by hills thickly wooded with the dark fir. It is one of the most popular spas of Europe, and, besides its permanent population of 15,000, it is visited in the summer by about 60,000 people. Moreover, the environs of Baden are most charming, and one can either begin or end a tour of the Black Forest at this point.

The average temperature of the year is 48.3° F., and for the summer as follows: May, 53.9° F.; June, 60.2° F.; July, 62.9° F.; August, 62.2° F.; September, 56.6° F. For the autumn, 47.6° F.; winter, 34.3° F. The yearly rainfall is quite large. The surrounding hills afford shelter from the cold winds in winter, but in midsummer they prevent the cool breezes from mitigating the heat which, for some persons, is too great for comfort.

The waters contain sixteen grains of common salt to the pint, at a temperature of 110° to 154° F. They are used for drinking, but chiefly for bathing, and in various forms of douches. The maladies for which such waters are recommended are rheumatism, gout, lithæmia, gastric catarrh, catarrh of the bladder, scrofula, chronic metal poisoning, obesity, and chronic catarrhal affections of the respiratory tract. The effect of the waters when drunk is diaphoretic, diuretic, and laxative. The bath establishments are extensive and well appointed, some of them luxuriously so, and include hot-air, vapor, pine, electric, and mud baths, and swimming pools. There is also an inhalation establishment, and a section for Swedish massage and mechanical gymnastics. There is an elaborate and extensive *Conversations-Haus* with pleasant grounds, and near at hand is a *Drink-halle*, most frequented in the early morning, when the waters are drunk to the accompaniment of music, the usual custom in European spas. There are also several private sanatoria under competent direction. The

sanitary condition of the city is satisfactory, and the water supply for domestic purposes comes from mountain wells. The accommodations are abundant, excellent, and of varying price. The baths are open all the year, although they are most frequented during the season (May to October). There are also milk, herb, and grape cures. The situation of Baden with its hills affords opportunity for the "Terrain-Cur." One can also make an "after-cure" here after a course of more active mineral waters.

East of Baden-Baden, in the northeastern part of the Black Forest, is Wildbad (1,410 feet), a much-frequented spa, containing indifferent thermal waters, of a temperature of 91.3° to 104.5° F., used very largely for bathing, although they are also used for drinking and gargling. The town, of about 3,000 inhabitants, lies in the narrow wild valley of the Enz, surrounded by hills covered with pines, and possesses an agreeable climate and excellent drinking-water. The mean yearly temperature is 46.5° F., and the mean monthly temperatures for the season are: May, 53.7° F.; June, 60.8° F.; July, 63.1° F.; August, 62.6° F.; September, 55.9° F. The waters are beneficial for the class of cases for which simple hot baths are appropriate, such as chronic rheumatism, gout, chronic joint pains, metal poisoning, scrofula, functional nervous affections, catarrh of the respiratory organs, nervous dyspepsia, convalescence from acute and chronic diseases, certain gynæcological affections, and chronic skin eruptions. The bracing mountain air found here also enhances the value of a visit to this resort. The application of the waters is chiefly in bathing, and they are conducted from the wells in a continual stream at their natural temperature. There are also electric, steam, and hot-air baths; massage and gymnastics. There are several bath establishments, the property of the Government, two excellent ones, the Great Bathhouse and the König Karls Bad, and others for the poor or those of slender means. There are a variety of outdoor amusements, such as fishing, shooting, and tennis; and, as in almost all these resorts so largely visited by English and Americans, an English church.

Not far from Wildbad is Schömberg (2,130), where is situated a sanatorium for pulmonary tuberculosis conducted by a physician formerly attached to the Falkenstein Sanatorium, and in a similar manner.

St. Blasien (2,530 feet), in the southeastern part of the Black Forest, has an excellent climate and situation, affording mountain and forest air, and is resorted to both in summer and in winter. There are pleasant walks among the forests in the neighborhood, and the paths are arranged for the "Terrain-Cur." There is a well-known sanatorium here, open the whole year for the open-air treatment of pulmonary tuberculosis.

At Nordrach (1,470 feet), near the centre of the Black Forest, is Dr. Walther's celebrated "Nordrach-Colonie," in a protected position, looking toward the south. The success of Dr. Walther in the treatment of pulmonary tuberculosis has given this place and name a world-wide fame; with the English, especially, this sanatorium is very popular, and the sanatoria, now so frequently being established in England, follow Dr. Walther's methods, and sometimes take the name "Nordrach."

The climate at all these open-air resorts in the Black Forest is practically the same: the air is fresh and pure, fairly dry and equable, and although cold in winter (mean winter temperature, 29.6° F.) it is sunny and there is protection from the wind. The mountain influence is also apparent, and the thickly wooded character of the country is not without value.

Badenweiler (1,450 feet), in the lower part of the Black Forest, is a popular summer resort and spa, and possesses great beauty of situation and an excellent climate, pure air with a moderate humidity of seventy per cent., and an equable, mild temperature. The mean average monthly temperatures are: May, 53.8° F.; June, 61.5° F.; July, 64.6° F.; August, 62.8° F.; September, 57.4° F. The yearly rainfall is about forty inches. Badenweiler is used much more for a climatic health resort than for its waters, which are indifferent thermal (of 84° F.). They are used in drinking, in gargling, and in baths, and for various maladies—gout, rheumatism, neurasthenia, chronic neuralgia, diseases of the skin, catarrh of the respiratory passages, dyspepsia, dysmenorrhœa, etc. There are two public bathing pools, the "beautiful marble bath," an open swimming pool, and bath-rooms in a number of hotels. The baths are sometimes artificially heated, and common salt is added to render them more stimulating. The milk and whey cures can also be taken here. The sanitary conditions of the town and the water supply are good. There is also a steam disinfecting apparatus. The accommodations are good in hotels and pensions. In the vicinity of Badenweiler are various resorts of different elevations which offer favorable climatic conditions.

Rippoldsau (1,856 feet) is situated in about the centre of the Black Forest near the Kniebis Mountains, in a thickly wooded valley, with typical forest scenery, rocky precipices, cascades, and the ever-present fir trees. The waters are gaseous chalybeate, containing bicarbonate of iron, sulphate of sodium, carbonate of calcium, and free carbonic acid gas. The waters are taken internally in anæmia, chlorosis, debility, dyspepsia, catarrhal conditions of the stomach and bowels, etc. Iron baths are also used from two springs containing a small amount of iron and rich in carbonic acid gas. Mud baths are used extensively here, and are said to be effective in chronic rheumatic swellings, various sexual disturbances such as amenorrhœa, spermatorrhœa, and impotence. There are also pine-needle, electric, and sand baths, with massage and gymnastics. The baths are heated by Schwarz's method, which consists of the introduction of steam into the double bottoms of the separate baths. There are two well-appointed bathhouses containing twenty-five bath-rooms. The yearly average is about thirty-five hundred baths. The water from some of the springs, viz., Josef's, Leopold's, and Wenzel's, are bottled and largely exported, as is also the salt (Rippoldsau salts). The accommodations are good. The rural simplicity of the place remains, many of the old-time costumes being still worn by the natives.

There are numerous other small spas and climatic resorts in the Black Forest, all attractively situated and affording opportunities for hydrotherapeutic treatment or open-air life in a fresh invigorating atmosphere. Indeed, a walking, bicycle, or automobile tour through this most picturesque region may well be considered a cure in itself for tired nerves and the mentally overworked; and the writer, from personal experience, can bear witness to the charm and restfulness of such an excursion: the air is so fresh and invigorating, the food so good, the country scenery so attractive, and the singing of the skylarks so sweet and seductive.

Edward O. Otis.

BRONCHIECTASIS.—Dilatations of the bronchi, either diffuse or circumscribed, are known as bronchiectases. They are of common occurrence and arise from a great variety of causes. In all cases, however, the essential cause of bronchial dilatation is to be found in a weakness of the bronchial wall or an increase of pressure within the bronchus, or in a combination of both these factors. Bronchiectases appear both clinically and pathologically in such a variety of forms that their classification is difficult. According to their etiology they may be divided into the following forms:

Bronchiectasis.
1. Congenital.
2. Atelectatic.
3. Vicarious.
4. Emphysematous.
5. Inflammatory.

General Morbid Anatomy.—The condition of bronchial dilatation may be single or multiple, one or more of the bronchi being affected. In some cases the entire bronchial tree is dilated (*universal bronchiectasis*). When but one bronchus is dilated the condition is usually found

in the upper lobes; when many are dilated the lower lobes are affected. Usually the bronchial branches of the third or fourth order are the ones involved; they not infrequently become wider than the main bronchi, and may often be followed out to the pleura, where they end generally in a sac-like terminal dilatation of somewhat greater width, as is seen in Fig. 5118, *b*). In other cases the terminations may be of normal width, or they may become narrowed. The smaller bronchi may at times alone be dilated, the lung on section resembling a very porous cheese.

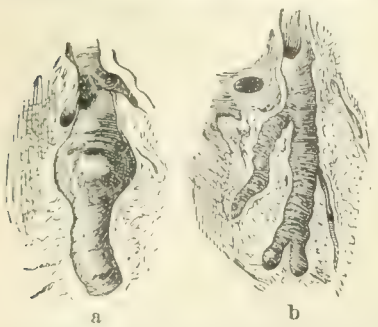


FIG. 5118.—Saccular and Cylindrical Forms of Bronchiectasis. (After Orth.) *a*, Saccular form; *b*, cylindrical form.

The dilatation may be more or less uniform (*cylindrical*, *fusiform*, or *spindle-shaped bronchiectasis*), or it may be localized, the dilatation being much greater at one point than elsewhere, or involving but a small portion of the bronchus (*saccular bronchiectasis*). In other cases a succession of dilated portions may be separated from each other by portions of the bronchus which are of normal width or are constricted (*varicose* or *rosary bronchiectasis*). The different forms may be found in the same lung. Closure of the central end of the dilated portion and the accumulation of secretions may give the dilatation the character of a cyst (*bronchiectatic cyst, cystic bronchiectasis*). Suppuration of the wall of the dilated bronchus gives rise to the conditions known as *ulcerative bronchiectasis* and *bronchiectatic abscess*. Enlargement of the bronchiectasis at the expense of the surrounding lung tissue leads to the formation of bronchiectatic cavities (*cavernous bronchiectasis*). Infection of the dilated bronchus with putrefactive organisms causes a *gangrenous bronchiectasis*. In this case also the destruction of the wall of the dilatation and the encroachment upon the surrounding tissue give rise to the formation of cavities. In some cases the larger bronchi may be chiefly affected, in which event the distended portions project from the main bronchus like the dilated fingers of a glove.

The walls of the dilated portion may appear to be normal, or they may show marked pathological changes. The inner lining may be smooth or roughened. The smooth-walled dilatations often contain no fluid. As a rule the bronchial mucosa presents the appearances of a chronic purulent catarrh. The cylindrical epithelium is usually replaced by one of a cubical or squamous type. In the large saccular bronchiectases and in some of the cylindrical forms due to retained secretions the lining membrane may be ulcerated. Polypoid outgrowths are not infrequently seen. The contents of the cavity may be thin and watery, or thick or even caseous. In some of the larger bronchiectases, and particularly in the case of secondary gangrene, the contents are horribly fetid. Microscopically the fluid consists of mucus, pus corpuscles, fatty acid crystals, and occasionally blood and hæmatoidin crystals. In the case of ulcerative or gangrenous conditions of the walls elastic fibres may also be present. The outer portions of the wall of the dilated portion may be markedly atrophic; even the cartilage plates may entirely disappear. The elastic tissue is stretched and separated; and the muscle, if it has not entirely disappeared, is much stretched and atrophied. The mucous glands may also entirely disappear, or may show extreme mucous degeneration. In other cases a secondary thickening of the wall, due to a new formation of connective tissue and elastic fibres, may occur. This is true particularly of the inflammatory cases. Small-celled infiltration of the wall is usually present. According to the condition of the bronchial wall bronchiectases may be divided into the *atrophic* and the *hypertrophic* forms. Such a classification has, however, but little practical importance, inasmuch as both forms may be found in the same lung. In general, the condition of the wall is dependent essentially upon the cause of the dilatation.

FIG. 5119.—Atrophic Cylindrical Bronchiectasis with ribbed transverse markings. (After Ziegler.)

The *atrophic form* occurs in association with emphysema, and as a sequela of old chronic inflammatory processes which lessen the elasticity and resisting power of the bronchial wall, so that it gives way to the air pressure. Prolonged and difficult expiration favors its occurrence. Such dilatations are usually cylindrical and occur chiefly in the bronchi of the lower lobes. Very often the stretching of the bronchial wall is not uniform, and the inner surface shows circular or oblique ribbed elevations corresponding to circular bands of muscle fibres and elastic tissue which are still preserved, the connective tissue between them being pushed outward. All the elements of the wall are more or less atrophic, even the cartilage, which may be replaced by connective tissue containing newly formed blood-vessels. The openings of the mucous glands are dilated and funnel-shaped. The epithelium may be well preserved, or it may be changed to a cubical or flattened variety, or may be desquamated.

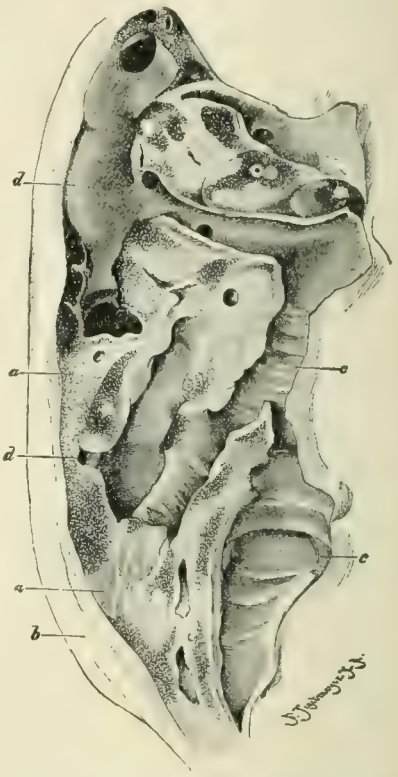


FIG. 5120. — Hypertrophic bronchiectasis and bronchiectatic caverns in fibroid induration of lung. (After Ziegler.) *a*, Indurated lung-tissue; *b*, thickened pleura; *c*, dilated bronchus; *d*, cavity communicating with a dilated bronchus.

The *hypertrophic* form occurs as a frequent sequela of indurations and contractions of the lung parenchyma. In these cases the greater part of the lung is usually impermeable to air, and the cause of the dilatation is less a result of the weakening of the bronchial wall, but is essentially dependent upon an increase of intrabronchial pressure, which is due to the fact that the air entering the bronchi no longer passes normally into the ramifications of the air passages. In the case of retraction of

the lung tissue with pleural adhesions the outward pull upon the bronchial walls is also an important factor in causing a dilatation of the bronchial lumen. In both cases the dilatation is favored by any inflammatory process which weakens the wall. The mucous membrane of the dilated bronchus in the hypertrophic mass may resemble that found in the atrophic forms, or papillary or polypoid proliferations may be present. A lattice-like marking of the lining membrane is often seen. These markings correspond to small thickenings or elevations of the mucosa corresponding to the formation of a very cellular granulation tissue about the longitudinal and transverse bundles of elastic tissue. The connective tissue of the wall and of the peribronchial region is more or less thickened and connective tissue may take the place of the mucous glands and cartilages. The capillaries of the wall are greatly dilated and present thickened walls. The hyperæmia of the wall may be so marked that the appearance of the mucosa suggests a hemorrhagic condition. Tuberculous and gangrenous processes may cause various modifications of these appearances.

The *saccular* bronchiectases usually develop at the cost of the lung parenchyma. The bronchus may show at some point in its course a dilatation varying in size from that of a mustard seed to that of a hen's egg, or the bronchus may terminate in a sac. The central end of the dilatation may become obliterated and the dilatation thus come to resemble a cyst. Through the accumulation of secretions the cyst may attain great dimensions. All the bronchi of one lung may be similarly affected, the lung tissue between becoming atrophic and compressed, so that the organ finally comes to resemble a multilocular cyst. In other cases the saccular dilatation may involve only a portion of the circumference of the wall, so that it appears as a diverticulum which is connected with the lumen of the bronchus by a narrow opening only (*dilatation ampullaire latérale* of Cruveilhier). In the majority of cases the saccular dilatations involve the smaller bronchi, more rarely are the main branches affected They are usually associated with bronchial stenoses, and are most often found near the periphery of the lung. According to Gairdner all the saccular dilatations are the result of ulcerative excavations of the lung tissue. This is true, however, of only a part of the cases.

Biermer divides bronchiectases, according to the character of their walls, into the following forms: (1) Dilatations with catarrhal swelling and relaxation of the bronchial wall. These are acute and occur chiefly in the lungs of children affected with chronic bronchitis. After the bronchitis has been cured the bronchial wall regains its old tone and elasticity, and the dilatation disappears. (2) Dilatations with hypertrophic walls. These affect the larger bronchi and are usually spindle-shaped. (3) Dilatations with thin walls. These are usually saccular. (4) Dilatations with trabecular degeneration. The walls are uneven, thickened, and there is a peribronchial increase of connective tissue.

Ulcerative processes are of common occurrence in the mucosa of the saccular bronchiectases. Complete destruction of the elements of the wall may take place, giving rise to a bronchial abscess. Infection with putrefactive bacteria leads to a secondary gangrene. Such changes are due to the lessened resistance of the bronchial walls, the changes in the secretions, and the entrance of bacteria. In these cases elastic tissue may be found in the sputum. Deposits of lime salts may occur in the bronchial walls, and as the result of the formation of granulating surfaces adhesions of the walls or the development of connective-tissue bridges may take place. In some cases a complete obliteration of the lumen results, and the bronchus is converted at the point of dilatation into a fibrous cord.

The changes in the lung tissue in the neighborhood of the bronchiectasis are usually primary, with the exception of ulcerative and gangrenous processes, which are secondary to the dilatation. The bronchi which are not dilated show catarrh and a putrid decomposition of the secretions. They are often wholly obliterated. In bronchiectases due to syphilitic affections of the air passages the dilatation of the smaller bronchi is usually secondary to a stenosis of the trachea or large bronchus. The portions of the lungs not affected by the condition causing the bronchiectasis may present a compensatory emphysema, and in the later stages foci of bronchopneumonia, due to the aspiration of secretions from the dilated bronchi, may be found. The right ventricle may become hypertrophied and dilated as the result of the stasis in the pulmonary circulation. The bronchial glands are usually swollen.

Metastasis may take place from bronchiectases. Biermer observed metastatic brain abscesses in four cases of bronchiectasis; and Gerhardt and Bardenheuer noted the occurrence of rheumatic joint affections in patients with bronchiectases. Chiari has reported a case of suppurative myelitis following bronchiectasis. In the pus and vessels of the cord a branching filamentous fungus was found which showed threads breaking up into coccoid bodies and staining with Gram's mixture. Of eight cases of hæmatogenous myelitis collected from the literature three were secondary to bronchiectasis. In one case of actinomycotic abscesses occurring in the brain of a man with numerous bronchiectatic cavities, many clusters of the fungus were found in the walls and contents of the latter.

Location.—Statistics as to the location of bronchiectases are of doubtful value. This is particularly true with regard to the relative frequency of involvement of the right and left sides and the upper and lower lobes. The statements generally made in regard to these points are to the effect that bronchiectases usually occur in one lung, and more frequently on the left than on the right side, and more often in the upper lobe than in the lower, and that in double-sided bronchiectasis both upper lobes are more often affected than the lower ones. But little importance can at present be attached to such statements, the number of observations upon which they are based being too small. The dilatations occurring with tuberculosis and chronic inflammatory processes are more often seen in the upper lobes; in the case of pleuritic exudations, in the compressed lower lobes; in those occurring as sequelæ of croupous and catarrhal pneumonia, hypostatic and atelectatic conditions are found in the lower and posterior portions. In the case of pleural adhesions the dilatations are sometimes found in the bronchi of the upper lobe, sometimes in those of the lower lobe.

Congenital Bronchiectasis.—Under this head there is included a number of conditions in the lungs of the newborn which have been regarded as due to congenital syphilis. One lung is usually affected; it may contain numerous cysts filled with a serous fluid. The lung tissue between the cysts may be indurated or atelectatic. Heller, Herzheimer, Grawitz, and others have described cases which, according to Grawitz, are to be ascribed to a hydropic dilatation of the bronchi. Heller regards them as representing the bronchi of undeveloped portions of the lung, the dilatation occurring in later life partly as the result of the growth of the thorax and the consequent pull upon the bronchus, and partly as the result of the growth of the bronchus itself and the pressure of retained secretions.

Atelectatic Bronchiectasis.—The congenital bronchiectasis of Heller is to be placed in this class. In a number of cases observed bronchial dilatations have been found in adults, the lung tissue being free from pigment and showing no evidences of inflammatory changes. The condition is therefore very probably the result of a congenital atelectasis. An acquired bronchiectasis, due to atelectasis, may take place in later life as the result of deformities of the thorax, tumors, aneurism, etc.

Vicarious Bronchiectasis.—If the entrance of air into any portion of the lung be hindered and the volume of that part reduced, the inspiratory pull upon the sound portions of the lung is increased. As the result of this increased pull both the alveoli and the bronchi become dilated, and there arise a vicarious emphysema and a vicarious bronchiectasis. Pneumonic foci, infarcts, local

atelectasis, local tuberculous nodules and infiltrations, contracting scar tissue, etc., are the causal factors of such bronchial dilatations. The bronchial wall and mucosa become stretched and thinned like a serous membrane. The essential characteristic of the change is that no inflammatory processes take part in the direct production of the dilatation. It is to be regarded as a vicarious emphysema of the bronchi. The clinical significance of the condition is not great. The dilatations are relatively small and circumscribed. Inflammatory changes may follow, and an ulcerative or inflammatory bronchiectasis develop.

Emphysematous Bronchiectasis.—An emphysema of the bronchi occurs also in simple atrophic emphysema of the lungs not due to a compensation for portions of the lung the function of which is lost or diminished. It is to be regarded as idiopathic rather than vicarious or compensating. The dilatation is not great, but the walls of the bronchi are greatly thinned. The smaller branches, particularly those of the lower lobes, are chiefly affected. The symptoms cannot be separated from those of alveolar emphysema.

Inflammatory Bronchiectasis.—This is by far the most common and important form. All authorities are agreed that for the production of a bronchiectasis of clinical importance an inflammatory weakening of the bronchial wall is necessary. In general there are no severe inflammatory conditions of the lungs or pleura in which bronchiectases may not develop. Capillary bronchitis, chronic bronchitis, catarrhal pneumonia, croupous pneumonia, particularly when running a subacute or chronic course, tuberculosis, obliteration of the bronchioles due to indurations, peribronchitis, typhoid hypostasis, stenosis of the large bronchi, pleuritis, pleural adhesions, etc., are the causal and predisposing factors. General anæmia, marasmus, alcoholism, excessive or forced respiratory movements, singing, screaming, coughing, etc., play a secondary part. In the case of bronchial stenoses the bronchus is usually dilated both above and below the point of stenosis. It is probable that the dilatation which lies below the stenosis is due to the fact that the air which passes through the stenosis into the portion of the bronchus below it is held there by the blocking of the stenosis with mucus during expiration, and as the result of the expiratory increase of pressure this portion of the bronchus becomes stretched. In the case of foreign bodies the bronchial dilatation is found not only around the body, but involving other bronchial branches as well. The causes of such dilatations are complicated, but the essential factor is the production of a peribronchitis. Tuberculosis and syphilis may give rise to bronchiectases which are primarily dependent upon stenoses caused by the contraction of scar tissue, or are due to infiltrations. Chronic pneumonia, whether following the acute pneumonias, or due to syphilis, pleuritis, foreign bodies, etc., or primary of unknown origin, is of especial importance in the etiology of bronchiectasis.

Symptoms.—*Cough.*—This is the rule. It occurs in paroxysms, usually at long intervals, almost always on the patient's awakening in the morning, the paroxysm being repeated once or several times during the day. The patient may be awakened by the first paroxysm, or it may come on after arising. Usually the patients know the time when the attacks may be expected. A paroxysm may also be precipitated by the patient's lying upon the affected side and then turning suddenly into another position. The attacks are often very violent and convulsive, at times completely depriving the patient of breath. The frequency and severity of the cough are dependent upon the position and the character of the opening of the dilatation. As long as the secretions are retained within the cavity there is no coughing, but when these escape into the neighboring bronchi and alveoli paroxysms are excited. When the bronchiectasis is located in the apex the secretions may pass continuously into a vertical bronchus and thus give rise to almost constant coughing.

Dyspnœa.—This may be slight or entirely absent; it usually increases in degree toward the later stages of the affection and may become very marked. Ordinarily it is noticed only at the time of coughing, or after vigorous exercise. It is increased in the event of acute catarrhs of the respiratory tract, and in the case of the collection of mucus in the smaller bronchi. Persistent dyspnœa is due to some complication on the part of the heart or lungs.

Expectoration.—The attacks of coughing are attended by expectoration. This may resemble that of any ordinary bronchitis, but in the majority of cases the expectoration is very characteristic and of diagnostic importance. With the coughing paroxysm there is a gush of sputum so great as to fill the patient's mouth. Within a few minutes an ordinary sputum cup may be entirely filled. The total amount of sputum may be so great as to suggest the possibility of the perforation of an empyema into the bronchus or lung. Five to seven hundred cubic centimetres may be expectorated within the twenty-four hours. With the evacuation of the dilatation the coughing usually ceases, to begin again as soon as the bronchiectasis fills up. Usually the sputum is raised easily, without much effort or coughing, but in the case of such complications as pleuritis, emphysema, tracheal or bronchial stenosis, etc., the expectoration may be very difficult. The position of the patient is of great importance; when he lies upon one side there may be neither cough nor expectoration, but as soon as he turns upon the other side the bronchiectasis begins to empty itself and the cough and expectoration are excited. Sensations of pressure, fulness, and pain are sometimes felt before the expectoration takes place, particularly in the case of children. Occasionally these symptoms may be very marked, lasting half an hour or so before the expectoration occurs. The large amounts of sputum and the long periods between the attacks of expectoration may be explained as due to a lessened irritability on the part of the bronchial mucosa, a larger quantity of sputum being necessary to excite coughing. The amount of sputum raised is always greater during the morning hours. Toward the end of the affection the total amount decreases as the patient becomes weaker.

Sputum.—The sputum is usually purulent in character, but may be fetid or gangrenous. When purulent it is yellowish and contains more or less mucus. If fetid in character the odor may be extremely disagreeable and penetrating, so that the patient's breath may be perceived some distance away. The patient himself shows a remarkable tolerance of the odor; nausea is rarely produced. In the gangrenous cases the sputum is grayish-yellow or greenish in color. When the complication of gangrene is not present the sputum may have no putrid odor, but commonly possesses a disagreeable, nauseating, acid or sweetish smell (pseudogangrene). When collected in a glass or cylinder the sputum separates into two distinct layers: an upper, thin, slightly cloudy, almost serous layer; and a lower, thick, purulent layer containing caseous masses. The latter appear as dirty yellow plugs varying in size from a mustard seed to a bean (plugs of Dittrich). If the sputum be put into a tall cylinder which is half filled with water, four distinct layers may be seen. The uppermost is foamy; the one beneath this consists of muco-purulent masses, which hang down in the form of shreds into the third layer, consisting of cloudy water. The lowest layer of water has a grayish-green appearance.

Microscopically the sputum is made up of pus corpuscles which may be well preserved or contain fat droplets. In the case of putrid decomposition bacteria, crystals of fatty acids, margarin, tyrosin, leucin, and triple phosphates may be present. Blood-pigment may also be found. In the case of gangrene elastic fibres may be present. The caseous plugs stain a brownish-yellow, blue, or violet with dilute iodine solutions. The mucin content of the sputum varies greatly. Blood cells are not infrequently present.

Hemorrhage.—The presence of blood in the sputum of bronchiectasis is not rare. The amount is usually small,

but the hemorrhage may be so large or so frequently repeated that severe symptoms or even death may ensue. The sputum in such cases may appear to be chiefly blood; it is rarely bright-red, but is more or less discolored by the mixture with the other elements of the sputum. The smaller hemorrhages are chiefly of capillary origin; the large ones come from the erosion of large vessels in the wall of the dilatation. In ulcerative conditions of the wall the hemorrhages may be very severe, persist for a long time, and finally lead to death.

General Symptoms.—When secondary changes in the heart, kidneys, etc., are not present, the general condition of the patient may be quite good or fair. Fever and sweating are signs of complications. Occasionally fever may be caused by the absorption of products of decomposition from the cavity. In such cases the fever does not present any distinct type.

Physical Signs—Inspection.—The color of the skin is usually unchanged. When it is very pale the underlying disease is most likely to be tuberculosis; when it is cyanotic there is usually emphysema present. Many of the patients lie upon their backs; others sit bending forward, claiming that this prevents the swallowing of the sputum. When the bronchiectasis is confined to one side, the patients usually lie upon the affected side, coughing and profuse expectoration being caused by turning upon the sound side. Deformities of the thorax are rare, occurring only in the case of retraction of the lung, or when extensive pleuritic adhesions are associated with the bronchiectasis. Diffuse or localized retraction of the thoracic wall and curvature of the spine may result from these conditions. When emphysema is present the thorax may present the characteristic barrel form. Occasionally differences of movement may be made out between the two sides. In the case of extensive bronchiectases of the lower lobe of of one side there may be seen during deep inspiration a wave-like retraction of the intercostal spaces proceeding from above downward. On the affected side such a movement is not visible. A compensatory emphysema of the sound lung is always found in such cases. Very rarely it may be seen that the respiratory movements on the affected side lessen, and at last wholly cease as the bronchiectasis fills up, but return after the expectoration has emptied the bronchus.

Among the most common and important of the physical signs of bronchiectasis are the changes which take place in the distal phalanges of the hands and feet (drumstick fingers). The clubbing of the fingers is due to a hypertrophy of the terminal portions of the bones (ostéoarthropathie hypertrophiante pneumique), so that the joints of the phalanges, the carpal joints, and even the wrist joint may be greatly thickened. These changes take place in association with chronic cyanosis and appear to be dependent upon the latter. They are also found in other conditions than bronchiectasis, particularly in the congenital heart lesions; but Bamberger has attempted to show that the change in bronchiectasis is characteristic of this affection, in that it is a painful hypertrophy of the epiphyses.

Percussion.—The percussion phenomena of bronchiectasis vary greatly, being dependent upon the size of the dilatation, the quantity of fluid present in it, its distance from the chest wall, and the character of the changes in the surrounding lung tissue. Dulness or a tympanitic tone may be obtained, or both alternately, according as the cavity contains fluid or air. A tympanitic tone with change of pitch on opening and closing the mouth may be noted, as well as change of tone on change of position, the cracked-pot sound, metallic tones, etc., according to the conditions present. About the areas showing such signs of cavity the tone may be resonant; in the case of tuberculous cavities it is always dull. The dislocation of the neighboring organs, pleuritic thickenings, adhesion, etc., may also be shown by percussion.

Auscultation.—The vesicular murmur is weakened or absent, being replaced by a bronchial blowing. The cylindrical dilatations give a soft bronchial sound, and when containing fluid they yield also moist, coarse bubbling râles. The saccular dilatations give both the percussion and auscultation signs of a cavity, particularly large, moist, bubbling râles.

Complications.—The most frequent and dangerous complication is the putrid or gangrenous decomposition of the contents of the dilatation. Pleuritis, peribronchitis, bronchopneumonia, chronic pneumonia, chronic bronchitis, lobar pneumonia, emphysema, chronic laryngitis, renal and cardiac affections, dropsy, albuminuria, cirrhosis of the liver, etc., may be associated with bronchiectasis or appear as sequelæ. Metastatic abscesses may occur in the brain, spinal cord, etc.; there may also be rheumatic joint affections. There arises in these cases a suspicion of the occurrence of a general pyæmic infection. Perforation of the dilatation into the pleural cavity leads to the development of a pyopneumothorax. In old chronic cases of long duration amyloid degeneration of liver, spleen, and kidneys may be found. Tuberculosis is a fairly common complication. The heart is usually affected, hypertrophy and dilatation of the right ventricle occurring in the majority of cases. The cardiac changes are due partly to disturbances in the pulmonary circulation, partly to the accompanying condition of chronic intoxication, partly to local changes in the thorax, and partly to coincident renal changes.

Duration and Course.—Bronchiectases may remain stationary for years, the only symptoms being those of a chronic bronchitis. As a rule the dilatation gradually increases during this time without an increase in the symptoms. With the advent of fresh catarrhs emphysema gradually develops, the shortness of breath becomes more marked, and the patient may become cyanotic. The right heart becomes hypertrophic and finally dilated. Putrid bronchitis and gangrene may occur; from these the patient may recover for a time, or death may take place. As a rule the condition runs for a long time; amyloid disease of the kidneys may finally result and the patient becomes dropsical. After alternating periods of improvement and exacerbation, extending over a long period, the disease is brought to an end by some one of the complications.

Diagnosis.—The differential diagnosis of bronchiectasis from its complications is sometimes very difficult. The absence of the tubercle bacillus will distinguish it from tuberculosis. When the latter process is combined with bronchiectasis the character of the sputum, the age of the patient, position of the cavity, habitus, etc., are points to be considered in the differential diagnosis. The history of the case is of greatest importance. It may be taken as a guiding principle that tuberculosis may lead to a bronchiectasis, but that a bronchiectasis rarely becomes tuberculous. Actinomycotic cavities may be distinguished by the presence of the fungus in the sputum. The rare localization in the lung of hydatids may also be easily diagnosed by the findings in the sputum. From pulmonary gangrene, abscess, putrid bronchitis, interstitial pneumonia, pyopneumothorax, etc., the differentiation is often impossible. The physical signs of cavity are of the greatest importance in so far as the differentiation between processes with cavity formation and those without is concerned. Much was expected from the use of x-rays in the diagnosis of bronchiectasis, but these expectations have not been realized. Only in the case of extensive peribronchial thickenings may aid be looked for by the use of x-rays.

Treatment.—In very rare cases self-healing of the bronchiectasis may take place. In children this may follow the cure of catarrhal bronchitis and the restoration of normal conditions of pressure. In extremely rare cases the bronchial cavity may be obliterated by adhesion of the walls of the cavity or through the formation of granulation tissue. Since in the great majority of cases such healing is impossible, the prophylactic treatment becomes of prime importance. The conditions (pleuritis, pneumonia, etc.) which lead to bronchiectasis should be appropriately treated with a view to the prevention of such dilatations. After the development of bronchiectases the chief therapeutic indication is to keep

the contents of the dilatation—so far as lies in our power—aseptic. This can be perfectly accomplished only by residence in an atmosphere containing no bacteria. Removal of the patient to a suitable climate is the best means of avoiding the various complications of the affection. When this cannot be done the treatment becomes chiefly symptomatic and largely directed to antiseptic procedures. Inhalations of creosote, turpentine, menthol, eucalyptus, etc., and creosote vapor baths are recommended for this purpose. A number of writers speak favorably of the creosote vapor baths. These are, however, unpleasant and slow in operation, and do not always succeed in lessening the amount of the sputum. The crude creosote appears to be more effective than the various substitutes (vapo-cresoline, refined creosote, soluble cresol, etc.) which have been advised. Other writers have found success with guaiacol vapor baths after failing with creosote. The ordinary methods of giving such inhalations may, however, be a source of infection, as many of the forms of inhalation apparatus used are dirt traps.

Intralaryngeal injections of menthol, guaiacol, etc., have been advised by Rosenberg, Stewart, Campbell, and others, but are condemned by various writers because they give rise to constitutional disturbances, fever, and violent cough.

Subcutaneous injections of guaiacol (1 in 5) and creosote (1 in 5) in olive oil have also been recommended. They may give rise to inflammation and necrosis at the point of injection.

Intravenous injections of formalin (25–50 c.c. of a 1 in 2,000 solution of formalin in decinormal salt solution) have also been tried without success.

Injections of carbolic acid and menthol directly into the bronchiectatic cavity have also been suggested.

Murphy's method of filling the pleural cavity with air or nitrogen to such an extent as to cause a collapse of the bronchial cavity has been tried with some success. The air should of course be thoroughly sterilized. About 170 c.c. of air or nitrogen are injected every second or third day.

Inhalations of oxygen may aid in reducing the odor of the sputum. Symptomatic treatment with expectorants (apomorphine, senega, ipecacuanha, etc.) may at times give relief or temporary improvement. Hemorrhage should receive appropriate treatment.

Inasmuch as the medical treatment is usually without avail, much had been hoped from surgical intervention in the treatment of bronchiectasis. This has now been given a very extensive trial, with complete failure in the majority of cases, and only partial success in the others. These unsatisfactory results are easily understood when we consider the facts that the dilatations are often multiple and bilateral, and that the pulmonary tissue is usually extensively diseased. Dangerous hemorrhages may result, and anæsthesia is in itself attended with danger in these cases. The uncertainty of the physical signs also contributes to the unsatisfactory results. Puncture of the bronchiectatic cavity with a trocar and drainage, incision and drainage, cauterization of the cavity, etc., are among the operative procedures advised. From the cases thus treated which have been so far reported, it would seem that under favorable conditions of life the outlook for patients with bronchiectasis is more favorable without operation than with it. Improvement of the technique of operations upon the lung may lead to better results.

The *postural* treatment of bronchiectasis is strongly recommended by Ewart (*Lancet*, 1901). While not regarding it as curative in advanced cases, he holds that no other treatment is so simple, so rational, and so effective. In a case so treated the relief afforded the patient was striking, the persistent pyrexia stopped, and the gushing character of the expectoration ceased. Ewart advises a continuous elevation of the foot of the bed of from twelve to fourteen inches. For brief periods a greater elevation may be resorted to with benefit.

PROGNOSIS.—In so far as a cure is concerned the prognosis in any well-established case of bronchiectasis is bad. Except in rare cases no method of treatment at present employed is of avail in effecting a cure. Some of the more acute cases in young persons may, however, be cured. In the chronic cases our present methods of treatment can only relieve the distress of the affection and prolong life. *Aldred Scott Warthin.*

CAMPHOR, POISONING BY.—An unwarranted belief in the innocuousness of camphor prevails in the community, referable, probably, to the safety with which it is used as an external domestic remedy for minor ailments and to its agreeable odor. This should not, however, blind the physician to its real and serious dangers when taken internally; for it may act as a poison either when eaten frequently in small quantities, as for headaches or colds, or when swallowed accidentally or intentionally once or more in large amount. It is true that fatal cases are very rare, but the symptoms are often most alarming, even when recovered from. The lethal dose of camphor is difficult to determine. The smallest dose known to have produced violent symptoms in an adult is 1.3 gm.; the largest dose known to have been recovered from is 15 gm. (Kunkel, Blyth). Camphorated liniments swallowed by mistake have frequently been the cause of severe cases of poisoning, the fact of the drug being in alcoholic solution allowing it to be absorbed and disseminated through the system more rapidly and in larger quantity than when swallowed in the solid form. The histories which I shall presently cite illustrate further the usual sequence of symptoms, and such relations as the early or late supervention of convulsions to the occurrence or absence of vomiting, this depending upon whether any large proportion of what was swallowed remained long in the stomach in a comparatively insoluble condition, or was promptly taken into the circulation. Attention is also called to the statement that when camphor has been swallowed, what is absorbed undergoes such a transformation that the odor of it is not appreciable in the urine or fæces (Kunkel); sometimes not even in the breath of the patient. Still, other authorities declare that the bodies of those dying smell strongly of the drug.

Full doses of camphor produce markedly exciting effects upon the brain and the medulla, especially when an alcoholic solution has been taken which favors rapid absorption. The earliest evidences of this stimulation are flushing of the face, a rapid succession of ideas, perhaps agreeable hallucinations, with a sense of lightness of motion and a desire to dance, in fact an intoxication. These manifestations are transient and may soon be followed by tonic cramps and epileptiform convulsions. To these may succeed sometimes paroxysmal tonic and clonic cramps with movements of rotation, followed by paralysis; or again deafness passing into sopor, coma, and death, the parts of the nervous system which are first excited being apparently finally paralyzed. The temperature is lowered, but the pulse and respiration vary (Brunton, Husemann). If the patient recovers, the memory is apt to be wanting for some hours. There are no characteristic lesions after death.

The following cases are fairly typical of poisoning by camphor: Davies reports being called at 3 A.M to a child of two years and eight months, who had swallowed solid camphor. He found it pale, with blue lips, a rapid pulse, and suffering from severe convulsions. Vomiting was induced and the ejecta smelled strongly of camphor. The child soon recovered in part from its condition of collapse, but the convulsions continued, and in the intervals the patient was semicomatose. A stomach-pump was then used and the stomach washed out with warm water, procuring some relief. In five hours castor oil was given, also bromide of potassium, three grains every three hours. Still no improvement; the convulsions continued all night and the child died at 9 A.M. of the next day. The amount of camphor taken was probably half a drachm. From its being solid the stomach-pump could not act upon it effectively.

Craig reports that a man who was a hypochondriac ate

about three drachms of pure camphor. About half an hour after swallowing it he was seized with giddiness and nausea, staggered on rising and seemed likely to fall. Still he was unable to vomit, and was relieved by drinking some water. He was free from pain, and lay down with a drowsy ringing in the ears. In three-quarters of an hour the giddiness and nausea had gone, but he felt as if he had been taken from his feet and were being carried through the air. He sat down at the dinner table, but became suddenly unconscious. He had general convulsions, which soon ceased, and the reporter says there was no deviation of the eyeballs, pupils equal and small and not reacting to light, knee-jerks exaggerated; breathing rapid, cyanosis followed by pallor. He was not unconscious for over five minutes. There was no odor of camphor in the breath. About two hours and a half after taking the camphor he vomited copiously, and brought up no blood and some camphor. There was no retention of urine. His memory was affected for an hour after other symptoms had disappeared.

Honman reports the case of a girl of eighteen, to whom he was called at 11 A.M. She was in the habit of eating camphor. He found her unconscious and irritable, with dilated pupils, cold extremities, pale face, epigastrium sensitive to pressure, pulse thready and uncountable, and the breath smelling distinctly of camphor. The stomach was washed out after an unsuccessful attempt to produce vomiting by sulphate of zinc. Ether was given subcutaneously with immediate improvement. It was learned that she had had camphor in her hand, and had offered it to her roommate at bedtime. She had vomited during the night and had taken brandy and water about 8 A.M. Convulsive movements now began and extended from the lower extremities to the body and upper limbs. The temperature rose to 100.3° F., and the pupils were dilated. She died at about 3 A.M. the next day. At the autopsy the only finding attributed to camphor poisoning was a high degree of congestion of the vessels of the dura mater and surfaces of the brain. The government analyst reported a small quantity of camphor in the stomach, but it is observed that none of the ejecta or dejecta had been saved prior to the doctor's arrival at 11 A.M.

In regard to the treatment of poisoning by camphor, the most important precept laid down is the earliest possible emptying of the stomach by tube, stomach-pump, or emetic. Hypodermic injections of brandy or ether may be used, with perhaps the alternate hot and cold douche.

J. Haven Emerson.

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CANTHARIDES, POISONING BY.—The poisonous action of this drug is ascribed chiefly to the proximate principle *cantharidin*, which is from twenty-five to thirty times as active as the powder. As the unassayed powder or the tincture is the form in which it is most apt to have been taken, it is difficult to determine the fatal dose of cantharidin. Blyth states that a young woman died from twenty-five grains of the powder, probably equal to one grain of cantharidin, while the smallest dose of the tincture known to be fatal (Taylor) is an ounce, equivalent to gr. $\frac{24}{100}$ of the proximate principle. Poisonous effects may also follow from external applications of the drug, in which they result from absorption, especially in feeble persons and children. Blyth says that the popular idea of the influence of cantharides as an aphrodisiac holds good only as to the entire cantharides, and not as to cantharidin, and he considers it probable that cantharidin is not the only proximate principle in the insect. It is also stated that cantharides may be eaten with impunity by fowls, while the flesh of the latter may produce symptoms of poisoning if eaten by human beings. Ogier tells us that a fatal result may follow poisoning by this drug after as long an interval as twenty-four hours; also that proof of the cause of death may be found in the presence in the intestine of minute glistening particles of the insect. Fatal cases are rare.

The symptoms due to poisonous doses are given as follows by Husemann, Kunkel, and Blyth: They are shown in disturbances of respiration and in convulsions from involvement of the nervous system, often with headache, dizziness, stupor, and delirium. In the alimentary canal there appear at once burning in the mouth and throat followed by pain on swallowing, salivation, vomiting, and diarrhœa, while there develop intense irritation, pain, and a condition of inflammation of the kidneys and urinary passages, in consequence of which occur in the urine albumin, casts, pus, and blood, with catarrh and croupous deposits from the vesical mucous membrane. These are associated with strangury, dysuria, painful erections, and priapism. Sometimes pregnant women have aborted.

The following fatal case is reported by Lhôte and Vibert. A man of about sixty took a quantity of cantharidin, estimated at about 75 cgm. He died twelve to fourteen hours afterward, the symptoms presented not being accurately known. Autopsy four days post mortem. The lungs were much congested; there was a little froth in the bronchi. Stomach empty; mucosa actively congested. Kidneys large, turgescent, and extremely congested; several large sanguineous effusions under the capsule; cortical and medullary substances gorged with blood and the mucosa of the calices and pelvis strongly injected. Bladder contained 4–5 c.c. of bloody urine; mucosa strongly congested and of an intense red; no ulcerations but many ecchymoses. Mucosa of the urethra likewise congested. On microscopical examination of the kidneys the glomeruli were found detached from their capsules, and separated from them by an exudate, in the midst of which were seen at certain points numerous round, nucleated cells. In the convoluted tubes the epithelial cells appeared glued together; they filled and distended the tubes. A material extracted from the viscera produced upon animals the effects of cantharidin, and its chemical reactions were characteristic of that substance.

The *treatment* of poisoning by cantharides must be symptomatic. The stomach should be evacuated, the stomach-pump or tube being used for the purpose if the mouth and throat are not inflamed; if they are inflamed, apomorphine should be injected hypodermically or an emetic should be given. Opium and hot sitz baths should be used to allay pain and strangury, and water and mucilaginous drinks given freely, but fats and oils are to be avoided.

J. Haven Emerson.

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CAROTID GLAND.—(Synonyms: Ganglion intercaroticum; Glandula carotica; Glomeruli arteriosi intercarotici; Nodulus intercaroticus.)

This little-known organ lies in the bifurcation of the common carotid artery, generally near the posterior side of the internal carotid just as it comes off the main trunk. In size it is about 1–3 mm. in diameter, varying considerably. Because of its great vascularity the color is pink For some time it was thought to be an epithelial organ developed similarly to the thyroid and thymus from the branchial clefts, but further study showed it to be of entirely different origin and nature. Its embryonal origin is later than the thyroid and thymus, and it is in no

way related to them, for it arises directly from the primary vascular *anlage*, and therefore is not an epithelial but a perithelial structure. The first step in its formation consists of a cellular thickening of the external posterior portion of the periphery of the embryonal carotid. At this time the cells, of epithelioid type, are not distinguishable from the cells of the vessel wall itself, and the gland anlage is recognized merely as a thickening of the cell mass at this point. This entire nodule is surrounded by the adventitia, and over it run nerve bundles from the vagus and cervical sympathetic. Very early in its development capillary vessels derived from the common carotid at its bifurcation enter the cell mass, and soon form glomerule-like collections, which with the rapidly increasing cell growth soon distinguish the gland from the vessel.

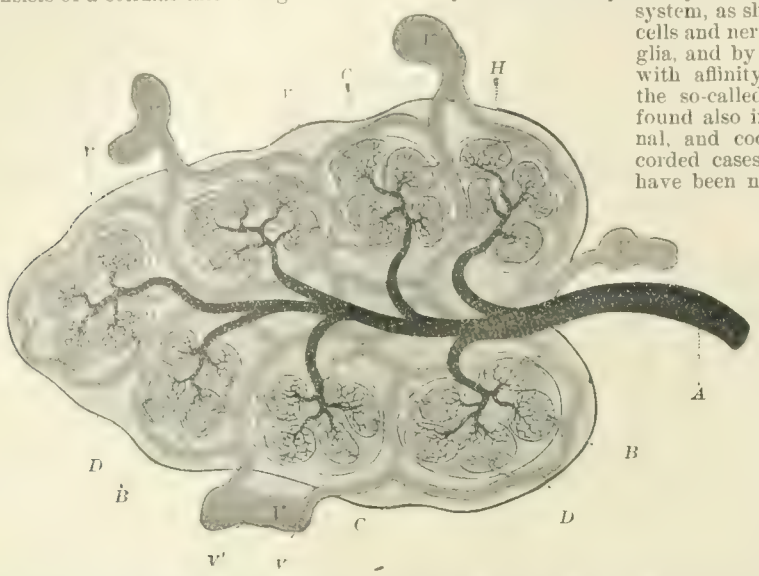

FIG. 5121.—Scheme of Circulation and Structure of the Carotid Gland, showing its Glomerule-like Character. (After Schaper.) *A*, Principal artery with *V*, corresponding vein; *B*, balls of cells; *C*, capillary networks; *D*, secondary nodules; *H*, hilus; *v*, *v'*, smaller veins.

In the adult the carotid gland shows a lobular structure. From the connective-tissue capsule bands pass into the organ carrying many vessels and nerves, and dividing it into lobules, which vary in number from three to twelve. In turn the lobules are composed of small "cell balls," which really form the unit of its structure. These consist of a glomerule-like tuft of capillaries that unite to form a vein. Surrounding the capillaries are the cells of the organ, arranged in cords or trabeculæ, although this arrangement is not at all evident in ordinary preparations. The number of cells about individual vessels varies greatly; sometimes there is quite a wall of epithelioid cells, with finely granular cytoplasm, oval nucleus, and a nucleolus, but often there is but a single layer of cells about a vessel, or the vessels may be separated merely by a loose reticular interstitial connective tissue. In this reticular tissue are frequently single cells of the same type. Often the parenchyma cells show a considerable degree of vacuolization, particularly in the old. It is said that with age the typical structure becomes less and less evident, accompanied by more or less disappearance of these special cells. The structure of the carotid gland is quite similar to that of the coccygeal gland.

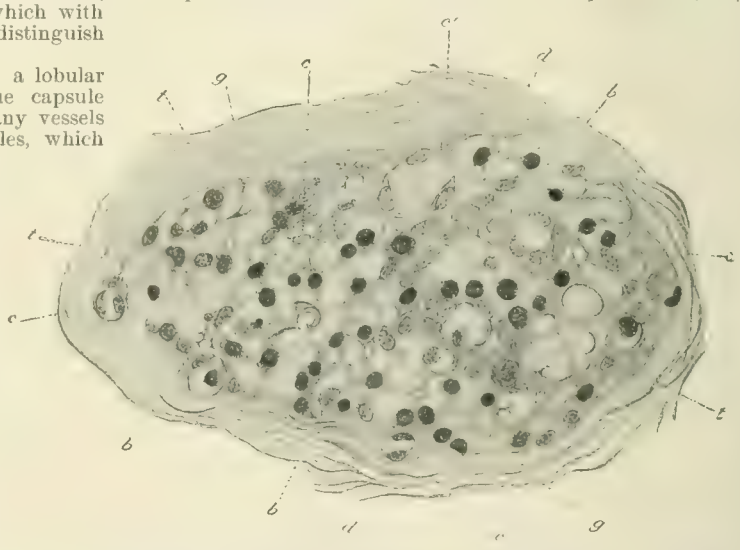

FIG. 5122.—Section of a Lobule of the Carotid Gland. × 520. From a man fifty years of age. (After Schaper.) *a*, Smallest arteriole; *b*, connective-tissue reticulum; *c*, capillaries; *d*, nuclei of stroma; *g*, protoplasmic network; *t*, nuclei of gland cells.

The function of the carotid gland is altogether unknown. It seems to have been the subject of but little investigation except by histopathologists. It is undoubtedly closely related to the sympathetic nervous system, as shown by the number of ganglion cells and nerve fibres from the cervical ganglia, and by the presence of the same cells with affinity for chromic acid and its salts, the so-called "chromophile" cells that are found also in the sympathetic glands, adrenal, and coccygeal gland. In the few recorded cases of tumors of this gland there have been no symptoms that could be considered indicative of any function, and the unilateral resection of the gland in these cases has been followed by no symptoms whatever. Extracts from the gland are said to raise the blood pressure greatly.

PATHOLOGY. — Except for tumor growths there seem to be no records of pathological alterations in this organ, probably because it escapes observation through its location and its minute size. There are in the literature eight cases of tumors of the carotid gland, all primary. They are characterized by their location in the crotch of the carotid, and by their peritheliomatous structure. They have appeared mostly about the thirtieth year, in either sex. In one instance the onset seemed closely related to fracture of the lower jaw in a tooth extraction. The growth is usually slow, in one about thirty years, and in none have metastases or recurrence been noted. All eight cases were observed through operative procedure, and there seem to be no records of such tumors discovered at autopsy. Subjective symptoms in these cases have been vague, such as headache, local pain, and tenderness. The tumor is quite fixed, because of its relation to the carotids, and for the same reason it frequently transmits pulsation which has led to a diagnosis of aneurism. In the other cases tuberculous cervical glands and thyroid tumor have been suspected.

Operation usually involves ligation of the carotid, which in one case led to death subsequently through the ligature cutting through the artery. In another case death resulted from broncho-pneumonia, which probably developed because of section of the vagus. The other six recovered completely, and seem to have remained well thereafter. In the two cases that were fatal, autopsy revealed no metastases whatever.

The malignant tumors of the carotid gland testify to its origin in the perithelium, for they form quite typical peritheliomas. The tumor is generally highly vascular,

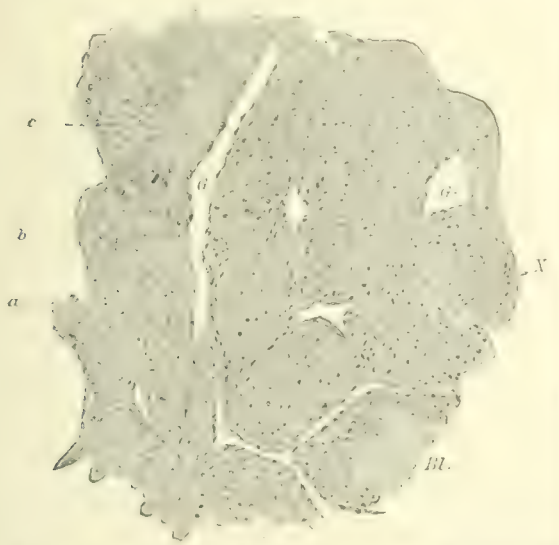

FIG. 5123. Perithelial Tumor of the Carotid Gland. After Paltauf. *G*, Vessels; *Bl*, blood extravasation; *a*, hyaline degeneration of cells; *b*, hyaline degeneration; *c*, hyaline masses.

and about the capillaries are layers of epithelioid cells, with a strongly staining oval nucleus, and considerable finely granular cytoplasm. The thickness of these walls seems limited by distance from blood supply, and the perithelial cells tend to form cords with central spaces lined solely by the tumor cells. The lobular structure of the gland is retained, as well as its richness in vessels and nerves.

Usually the tumor lies in the crotch of the carotid, "like a meal sack." The largest tumor reported is that of von Heinleth, which measured $3.5 \times 5 \times 8$ cm., and was 21 cm. in circumference.* *H. Gideon Wells.*

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CHYLOTHORAX.—This is a condition in which the pleural cavity contains chyle, due to a break in the continuity of the wall of the thoracic duct or its branches, or to some pathological condition of their walls whereby the contents may be transuded into the pleural cavity. Other writers give the name chyliform to those fluid exudates, in the pleural cavity, which contain fat in smaller amount than is found in the cases belonging to the class first mentioned. Furthermore, as these so-called chyliform fluids accompany tumors of the pleura in many cases, these writers believe that the fat comes from a fatty degeneration of the tumor cells. In a third class of cases the fat of the pleural fluid is supposed to result from lipæmia. In the latter cases the amount of fat contained in the fluid in the pleural cavity is small. Nevertheless, in many cases it may be difficult to differentiate these fluids from true chyle containing a small amount of fat and resulting from some definite lesion of the thoracic duct.

As stated, true chylothorax results from some definite lesion of the thoracic duct or its branches; but since lesions of this organ are not common, and since all lesions of the duct are not followed by chylothorax, the presence of chyle in the pleural cavity is an unusual condition.

Many of the older writers confused chylothorax with empyema or with the fibrinous exudates accompanying certain cases of pleuritis, and consequently some of the cases reported by these men, when studied carefully now, are found to be of a nature different from true chylothorax. It being assumed that this statement is correct, it appears that only forty-seven cases of genuine chylothorax have been reported, besides about fifteen others which are doubtful cases.

ETIOLOGY.—In the undoubted cases the age varied from 2 to 62. Two cases occurred in patients under 10 years of age; 8 in patients from 11 to 20; 7 from 31 to 40; 8 from 41 to 50; 3 from 51 to 60, and 2 after 60. From this it can be seen that the greatest number of cases occur between the ages of 11 and 51. This is explained by the fact that individuals between these ages are more exposed to injuries, or are more subject to new growths—conditions which are frequent causes of chylothorax.

In 41 of the undoubted cases in which the sex was given, 31 were males and 10 were females.

Chylothorax may result from obstruction to the flow of chyle through the thoracic duct, due to pressure from without by new growths or by tuberculous lymph nodes in the mediastinum. The obstruction may also be due to occlusion of the lumen by secondary new growths or to the presence of thrombi in the duct or in the left subclavian vein—in the latter case obstructing the mouth of the duct. Finally, it may be due to the presence of filaria. In other cases chylothorax results from pathological changes in the duct wall or from traumatic injuries to its walls.

Of the undoubted cases 16 resulted from injury to the chest; 9 from pressure exerted upon the duct by new growths outside the duct or by tuberculous lymph nodes; 9 from secondary growths in the duct; 4 from thrombosis of the left subclavian vein; 2 from proliferating lymphangitis; 2 from aneurism-like dilatations of the duct, and 1 each from the following: thrombosis of the duct, operation for removal of carcinomatous lymph nodes of the neck, obstruction to the radicles of the duct from inflammatory thickenings in the mesentery, mitral disease, and filaria. All of these causes either produce a break in the continuity of the endothelial lining of the duct or put the endothelial cells under such abnormal conditions that their nutrition is impaired, and consequently they allow the transudation of the chyle.

SYMPTOMATOLOGY.—The symptoms of chylothorax which result directly from this condition are not characteristic. For the most part they resemble those of hydrothorax or a pleuritic effusion. In most cases the chief, and sometimes the only, symptom is a gradually increasing dyspnœa. In fatal cases this may be accompanied by a rapidly progressing emaciation, although the patient may have a good appetite and may eat well. A few of the patients complain of pain in the affected side if the chylothorax is unilateral, and of a general, indefinite, dull pain in the chest if the condition is bilateral. On inspection lagging of the affected side will be noticed and the intercostal spaces will be more or less obliterated. If the quantity of fluid is large, the heart may be displaced away from the fluid. Palpation reveals a lessened or entirely absent vocal fremitus, depending upon the amount of fluid

*Since this article was written there has appeared still another report of a tumor of the carotid gland by Reclus and Chevassu, (Revue de Chirurgie, 1903, xxiii., Nos. 8 and 9). This article also includes a full review of the subject to date, with particular reference to operative intervention, which these writers consider, is not indicated unless the tumor is causing much disturbance, since it is probably not malignant and resection involves injury to such important structures.

present. Percussion always gives a dull note on the affected side of the chest, both laterally and behind, the line of dulness being higher in front and lower in the back when the patient sits up, and reversed when the patient lies down.

In seventeen of the forty-seven cases chylothorax was accompanied by chylous ascites, and in one instance by chylopericardium. In one case there was chyluria, and in another milky diarrhœa.

The symptoms referable to other organs are usually due to the same pathological alterations as those which have brought about the chylothorax. In cases of external injury to the duct very few symptoms other than those mentioned appear.

Diagnosis.—The only evidence upon which a positive diagnosis of chylothorax can be based is that afforded by an examination of the fluid. This fluid, as withdrawn by an aspirator, is usually semitranslucent, milky, and opalescent. Its specific gravity is 1 020 in most cases. If allowed to stand, the fluid separates into two layers, an upper, slightly more yellow in color, and resembling cream in consistence, and a lower one, watery in character. If the whole is well shaken and extracted with ether or treated with sodium or potassium hydrate, the fluid becomes clear and loses its milkiness. Chemical examination of the fluid shows that from ninety to ninety-nine per cent. is water. Of the solids, the fat varies from 0.02 to 0.92 per cent.; salts and albumins, and sometimes a small amount of sugar, forming the remainder.

Prognosis.—In many cases the prognosis of chylothorax is good. In those which are due to obstruction, the anastomoses of the thoracic duct may do compensatory work, and thus the condition may be relieved. In cases due to injury to the duct from external causes, proper treatment frequently brings about a cure.

Treatment.—For those cases in which the chylothorax is due to some chronic obstruction, aspiration of the fluid, accompanied by rest and nourishing food, is about all that can be done. Cases due to injuries of the chest are treated in a similar manner.

In cases due to injury inflicted during an operation for the removal of carcinomatous or tuberculous lymph nodes in the neck, the duct may be ligated, resected, or packed, all of which procedures have been used.

Frederick A. Baldwin

Most of the literature of chylothorax is given by Bargebuhr, Deutsches Arch. f. klinische Medicin, 1895, liv., 410, and by Shaw, Journal of Pathology and Bacteriology, 1900, vi., 339.

DISSOCIATION, DIFFUSION AND ACTION OF SALTS.—The advance of physical chemistry in the last fifteen years has thrown a new light upon the behavior of salts in the tissues, and promises to form the basis of the explanation of their presence in all forms of living matter, as well as of much of their therapeutic value. The chief phenomena bearing on biology and medicine are the dissociation of salts and their relation to diffusion and osmosis, and before the results of the application of physical-chemical methods to the biological sciences can be appreciated some knowledge of the recent advances in the theory of these phenomena is requisite.

Dissociation, Ions.—It was formerly held that common salt dissolved in water remained in the same form as that which is familiar in the dry state, the only difference being that crystals divided into molecules. It is now recognized, however, that not only are the molecules isolated from each other, but that a certain number of molecules undergo still further division. The products of this molecular division are known as *ions*, and in the case of common salt are Na ions and Cl ions. The amount of dissociation that occurs varies with the strength of the solution; the weaker the solution the greater the percentage of salt undergoing dissociation. In a one-per-cent. solution of sodium chloride only about one-fifth of the salt is present in the form of molecules, the rest having dissociated into the two ions. These ions are not to be confused with atoms, for although sodium and chloride ions are present, the solution of course possesses none of the properties of metallic sodium or of free chlorine. The ions differ from the atoms in carrying a charge of electricity, the charge of the sodium ion being positive, while that of the chloride ion is negative.

If a battery be connected with the solution the sodium ions hurry to the negative pole or cathode, while the chloride ions give up their charge at the positive or anode. The sodium ion is therefore known as the *cation*, the chloride as the *anion*. At the moment at which the charge of an ion is given up the ion changes to an atom, but it immediately forms fresh combinations with the water, in the present instance NaOH and HCl.

Other salts undergo a similar dissociation in solution in water: KBr forms K and Br ions; $NaNO_3$, Na and NO_3 ions, K_2SO_4 divides into three ions, two potassium and one SO_4; ammonium oxalate forms two NH_4 ions and one oxalate anion, and so forth. The dissociation of acids and alkalies is of great importance, but resembles exactly that of the other salts, acids forming hydrogen cations and the rest of the molecule forming the anion, while alkalies divide into a hydroxyl anion and a metallic cation; HCl thus becomes hydrogen and chloride ions; NaHO, sodium and hydroxyl (HO) ions.

The ions in a solution are in constant motion, and the anions and cations of a substance in solution lose the connection which they possess in the solid state. Thus, when potassium bromide and sodium chloride are dissolved together in a sufficient amount of water, it is no longer correct to designate the result as a solution of potassium bromide and sodium chloride, for the potassium ions are in no closer connection with the bromide than with the chloride ions. The bodies present are really the potassium and sodium cations and the bromide and chloride anions. In the blood serum, for example, the phosphate ions present are not combined with the potassium nor the chloride with the sodium, but all four are independent, and it is incorrect to speak of the potassium phosphate of the blood serum. When a dilute solution of sodium hydrate is swallowed it is neutralized by the gastric juice, and the reaction is often stated as the formation of sodium chloride and water. In reality the hydrate solution contains sodium and hydroxyl ions, the gastric juice hydrogen and chloride ions, and the resultant fluid contains sodium and chloride ions. The change consists in the disappearance of the hydrogen and hydroxyl ions which have formed water, the chloride and sodium ions having been present to begin with and remaining unchanged.

Dissociation occurs in salts, including under this term acids and alkalies, but it is not developed equally in all salts. Those acids and bases which are generally considered to be the "stronger" dissociate more readily than the weaker combinations, and the monovalent salts more readily than the bivalent. The inorganic salts dissociate more readily than the organic, and the same holds true for the bases. All of those bodies in solution serve as electrical conductors; in fact, the passage of electricity through watery solutions is only possible through the presence of ions, and the conductivity of solutions is thus a measure of the degree of dissociation. Those substances which are dissociable are therefore known as electrolytes. On the other hand, many organic substances are incapable of conducting electricity and are also incapable of dissociation. Thus alcohol contains an hydroxyl (— OH) in combination with ethyl (C_2H_5), as sodium hydrate contains an hydroxyl in combination with sodium. Alcohol is, however, incapable of forming ions, and therefore is a non-electrolyte in aqueous solution, while sodium hydrate dissociates readily into hydroxyl and sodium ions, and these are capable of conveying an electric current.

Sodium hydrate has a characteristic action in the tissues, causing corrosion. This might be due to either the sodium or the hydroxyl ion. As a matter of fact, however, the sodium ion is present in many solutions which are devoid of corrosive effects, for example, in solutions of sodium chloride. The conclusion, therefore, is that the hydroxyl ion is the corrosive in this case. Alco-

hol has no such corrosive action as sodium hydrate, and this corresponds with the fact that alcohol is not an electrolyte, *i.e.*, does not liberate the hydroxyl ion, although it contains hydroxyl. Many other similar examples might be cited, all going to show that in many instances the therapeutic effects of a body are due, not to the molecule administered, but to the ions into which it dissociates in the fluids of the body. In fact in administering an electrolyte, the physician gives not one but two or more substances, which may each effect changes in the organism. As a general rule in therapeutics one ion is so powerful that the other may be neglected; for example, in morphine sulphate the alkaloidal cation is so active that the sulphate ion may be ignored, and the sulphate has therefore the same effect as the hydrochlorate of morphine. When the two ions are more equal in pharmacological activity, however, each has to be taken into consideration; for example, magnesium sulphate dissociates into magnesium and sulphate ions, each of which has a retarding influence on absorption in the bowel, while magnesium chloride similarly forms magnesium and chloride ions, of which the latter is indifferent in the bowel. The sulphate of magnesium has thus a more powerful purgative action than the chloride, and is also more active than sodium sulphate, which forms the purgative sulphate and the indifferent sodium ions.

Another example of the importance of ions to the understanding of therapeutic action and to its successful practice is offered by the bromides. Potassium and sodium bromides have a depressant action on the central nervous system, and as this is absent in the case of the chlorides of these metals, it is obviously due to the bromide ion. Bromated camphor also contains bromine in chemical combination, and attempts have been made to substitute it for the bromides as a depressant. But bromated camphor does not dissociate and no bromide ions are formed, so that whatever properties it may possess, it cannot be compared with the bromides of potassium or sodium.

The action of salts depending on the ions, the intensity naturally varies with the rate of dissociation. This is well exemplified in the local effects of the heavy metals; such salts as the chlorides and nitrates, which dissociate readily, are much more active locally than the sulphates and organic salts which divide into ions less rapidly, provided, of course, that all are equally soluble and have no special characteristics, such as deliquescence. The newer views as to the dissociation of salts and the important rôle of the ions explain why such bodies as the ferrocyanides have the effects neither of iron nor of cyanides, for neither iron nor cyanide ions are formed from them in solution. Similarly the cacodylates differ from arsenous salts because they do not liberate the arsenous ion except after decomposition in the body. Now in the case of potassium arsenite, the arsenite ion is the active constituent, and the cacodylates can possess this only when they are broken down in the tissues into arsenous salts. The slowly dissociating salts are thus often used to avoid the local action of the more irritant metals: for example, many of the recent compounds of iron have the advantage over the older salts of causing less local irritation, while they have practically the same effect on the blood formation. Similarly several new preparations of mercury have been introduced with the view of lessening the local action on the stomach and bowel, or of lessening the irritation induced by the hypodermic injection of mercury. These compounds, when soluble, are more slowly dissociated than corrosive sublimate, and, there being fewer mercury ions present at any one time, the local irritant action is accordingly reduced.

The disinfectant action of the heavy metals also depends largely upon ionization, for the destruction of the germs is due to a chemical reaction between the metal and the protoplasm of the microbes; and the larger the number of free ions the greater the tendency to union. The attempt has been made to obtain germicides devoid of the local irritant action by forming less readily dissociating salts than those in ordinary use. A large number of preparations have thus been introduced, partly compounds with organic acids, partly with proteid bodies. But as the irritant and the germicidal action of most metallic compounds depend on the same factor, namely, the free ions, it seems likely that the lesser degree of irritation induced by these is obtained only by the sacrifice of much of the disinfectant value.

The double salts are much less readily dissociated than the simple, and not infrequently appear to liberate somewhat complicated ions, as in the case of the ferrocyanides noted above. They are therefore largely devoid of the local action of the parent substances, and this may be taken advantage of in therapeutics occasionally.

When two salts which have one ion in common are dissolved together in water, the dissociation is considerably reduced. For example, if corrosive sublimate be dissolved along with sodium chloride, the former is less dissociated than if it were dissolved alone in the same amount of water. In accordance with this general rule, it is found that the addition of sodium chloride to a mercuric perchloride solution lessens both its irritant and its germicidal power, and in cases in which it is desirable to mitigate the former, and in which the latter is of no importance, as in the treatment of syphilis by the hypodermic method, this mixture may be used instead of the pure mercuric salt.

The complete treatment of the dissociation of salts would involve a large part of pharmacology and therapeutics, in which the importance of the phenomenon is daily becoming more evident. The inorganic materia medica is more dependent on the principle than the organic, as the dissociation is much more complete in the former. It is possible to exaggerate the importance of the new law, however, for many of the facts and principles of therapeutics remain unaltered by its introduction. For example, it is undoubtedly more in accord with modern theory to attribute the effects in epilepsy to the bromide ion than to the bromides, as was formerly done, but this is after all a matter of nomenclature, and it is perhaps necessary at the present time to remember that there was a science and practice of therapeutics before the ion theory was broached. On the other hand, there can be no question that it has thrown much light on many questions, and removed many misconceptions. In the case of the bromides, for example, it is scarcely possible to maintain at the present time that the bromide of ammonium is superior to that of sodium, except possibly in regard to the local action on the alimentary tract, for in each case the active constituent is the bromide ion, and this is equally readily furnished by either salt.

In physiology and biology generally the theory of ions is of great importance, as is at once apparent from the fact that the fluids and tissues of the body can only conduct the electric current through the presence of ions. Every electric stimulus causes a change in their distribution, and every electrical discharge (and electrical changes accompany every movement and every other form of activity) is intimately connected with the presence of free ions, and in fact is possible only in their presence. The whole of electro-physiology, and naturally of electrotherapeutics, has thus to be based on the ionic theory, and the fact that every life process so far investigated has proved to be accompanied by electric changes indicates that the presence of free ions is necessary to life itself. This of course agrees with the fact that inorganic salts are present in every living tissue.

Not only do living tissues require the presence of free ions, but even dead colloid material is altered very remarkably by them. And certain facts have recently been brought out in regard to the dependence of the proteids on certain ions which promise to have a far-reaching influence on biology and hence on medical science. It has long been known that many proteids, notably the globulins, are precipitated from solution when such salts as the sulphates of magnesium or ammonium are added to them. But Hardy has recently shown that the precipitation and solution of colloids, such as the proteids, depend largely on the valency of the ions present in the solution. Thus

bivalent cations precipitate some colloids in comparatively small quantities, and trivalent cations are still more efficacious, while monovalent cations tend to keep them in solution or have a very much smaller precipitating action. The bivalent and still more the trivalent cations thus tend to oppose the monovalent cations in regard to colloid solubility; and as ions are necessary to the life phenomena, the monovalent must be counterbalanced by the bivalent in the tissues, for either of these alone would tend to change the colloids from the normal condition to one of excessive or deficient fluidity.

A good deal of interest has been aroused in regard to the antagonistic action of ions in living tissues, which is found to present some similarity to that described by Hardy in dead colloid matter. The organ examined with most care in this relation is the frog's heart, a very sensitive reagent to changes in its environment. It has long been known that the excised frog's heart will beat for a long time when supplied with oxygenated blood or serum, and also in fluids containing no organic matter, but merely the inorganic salts of serum. On the other hand, solutions of non-electrolytes, such as sugar, fail to maintain the contractions. The presence of ions in the perfusing fluid is therefore necessary to maintain the heart in activity. But all ions are not equally efficient, for a certain amount of sodium chloride is found to maintain the contractions longer than any other single salt. The contractions very soon become weaker in sodium chloride solution, however, and finally the heart is arrested. But this arrest may be prevented if the solution contain in addition to sodium chloride a trace of a calcium salt; on the other hand, a heart which has ceased to beat in sodium chloride solution may be induced to resume its pulsations if calcium be added to the perfusing solution. This phenomenon was first noted by Ringer,* and has been confirmed by all subsequent observers; but views differ as to the interpretation to be given it. Howell has upheld the theory that sodium and calcium are both necessary to the heart, and that when sodium chloride solution is perfused alone, the calcium in the heart muscle diffuses out and is washed away and the heart ceases from its losing one of the necessary constituents, calcium. In support of this view he has shown that when the lime ions are removed by other means, *e.g.*, by precipitating them with oxalates, the heart ceases to beat.

Loeb, on the other hand, holds that the heart can only beat in solutions of electrolytes, and that the least poisonous of these is formed by sodium and chloride ions. Even these are not altogether harmless, however, and after a time the heart ceases from poisoning with the sodium ion. Calcium ions are antagonistic to sodium, and the addition of lime salts therefore reinstates the contractions. To put it shortly, the heart ceases in sodium chloride solution because, according to one view, a necessary constituent, calcium, is all washed out, according to the other, because the sodium is poisonous and has to be antagonized by the lime. Loeb's view appears, at first sight, the less plausible of the two, because it has been held that sodium chloride is a perfectly indifferent substance to animal tissues. It must, however, be remembered that here there is always sufficient calcium present to neutralize any poisonous action of the sodium, and this argument has therefore little weight. On the other hand, he has brought forward some very telling facts in its favor in his investigations of other organs than the heart. Without going into all of these, it may be mentioned that he found striated muscle undergo irregular twitching contractions in sodium chloride solution, but these were arrested by calcium and other bivalent salts, so that the phenomenon is not confined to the heart muscle. Loeb found a small fish, fundulus, which lives in sea water or in distilled water indifferently, but dies in a solution of sodium chloride of the same density as sea water. This can only be interpreted as indicating that there is something present in sea water which prevents the poisonous action of sodium chloride. On investigating the subject further he found that in a solution of sodium chloride, to which traces of calcium salts were added, the fundulus and its eggs lived as well as in sea water. The conclusion is inevitable that the lime normally present in sea water antagonizes the poisonous action of sodium chloride in this case. The parallel between the behavior of this animal and that of the frog's heart and other organs is so close as to form an important support for Loeb's theory of the interaction of the ions. It may be added that numerous examples of a similar antagonism are already known in more complicated ions than sodium and calcium. Thus the antagonism of atropine and pilocarpine, of curarine and physostigmine in striated muscles, and of the central nervous depressants and strychnine is similar, although these differ in not being essential to the function of the organs on which they act.

It is to be noted that in the case of fundulus, the action of sodium chloride is antagonized by a comparatively minute amount of calcium, and also by corresponding small quantities of other bivalent and trivalent ions, such as those of barium, strontium, lead, zinc, chromium, and alum. Similarly calcium removes or lessens the poisonous effects of potassium salts on the heart, and the potassium ion is also necessary to the normal contraction, so that the antagonism is believed by some observers to be related to the valency of the metallic ion. The fact that electrolytes are necessary to the heart and other organs suggested to Loeb and Mathews the view that the antagonism is due, at any rate in part, to the electric charge carried by the ions, but this is very far from being proved or from being generally accepted. For it has been found that striated muscle, which undergoes abnormal contractions in solutions of several monovalent salts, fails to do so in all; and while the contractions are arrested by some bivalent metals, others have not this effect. The conclusion seems justified that the antagonistic effects are not immediately associated with the valency or the electric charge, but are the results of some unknown special relation between the ions and the protoplasm, these relations differing in different organs and for different metals. In other words, the calcium-sodium antagonism appears to be of the same nature as the atropine-pilocarpine one, and is equally inexplicable in the present stage of knowledge.

While each of the cations alone is poisonous and has to be antagonized by some other cation, ions are necessary to the life processes. Protoplasm can exist then only in the presence of a number of different salts, of which the chief liberate sodium, chloride, calcium, and potassium ions. The poisonous effects of sodium are counteracted by very small quantities of calcium, the ratio obtaining between those in the best media being about 1,000 to 1.

An electric current can be conducted through a watery solution only by means of the ions at liberty in it. The extent of dissociation in the fluid may therefore be estimated by the conductivity of the solution or inversely by the resistance met by the current. As long as there is only one salt in solution the calculation is simple and the results are unequivocal. And however many bodies are in solution, the amount of dissociation may be estimated, although if large amounts of undissociable matter (non-electrolytes) be present the results are too low. But such estimations give no clew to the nature or relative amounts of the salts in solution. Some efforts have been made to apply this method to the examination of the urine and the blood in the hope that light might be thrown on the condition of the kidney by its means. As a matter of fact, however, the urine is much too complex in its composition to permit of results of much value being obtained. The chief electrolytes here are the chlorides, and a small variation in their percentage may induce a large deviation in the resistance, while if the chlorides vary in one direction and the other salts in the opposite, the resistance may remain almost unchanged in spite of great alterations in the composition of the urine. The

* Ringer's solution, which has been widely used in physiology as that most suitable for conserving the life of tissues, contains sodium, potassium, calcium, chloride, phosphate and carbonate ions and is made up of 100 c.c. of 0.75 per cent. NaCl, 5 c.c. of 0.25-per-cent. KCl, 2.5 c.c. of 0.5-per-cent. $NaHCO_3$ and 0.75 c.c. one-per-cent. KCl.

chief non-electrolyte is the urea, and its presence in large amount may increase the resistance without any marked change in the amount of salts or their dissociation having occurred. The method cannot therefore be regarded as replacing the chemical analysis of the urine, for its results are of a totally different kind. And it has not been shown by observation that the results obtained by measuring the electrical resistance can be utilized for diagnosis or to indicate the value of therapeutic measures.

Diffusion and Osmotic Pressure.—When distilled water is carefully poured upon a solution of sugar so that the two liquids do not immediately mix, the sugar molecules soon begin to penetrate into the pure water, and after a sufficient lapse of time the contents of the vessel become homogeneous, the percentage of sugar in what was distilled water being the same as in the part corresponding to the original solution. The explanation is that the molecules are in constant movement and, diffusing in all directions, some of them penetrate into the pure water, and this process goes on until the latter contains as many particles as the original. The movement still continues, but now as many molecules diffuse back into the lower layer as into the upper so that equilibrium is maintained. The process is the same as that seen when a crystal of sugar is dissolved, for here also the constituent molecules leave each other and wander throughout the fluid.

When a membrane is stretched between the two fluids, the result varies with its character. If the membrane offers no resistance to the passage of water and sugar, the same phenomenon is observed as if they were not separated by a membrane; the fluid on each side becomes homogeneous, although this generally takes more time, owing to the fact that currents are less liable to aid the process. If the membrane be permeable to neither sugar nor water, of course the fluids remain completely isolated and unchanged. On the other hand, some membranes, known as semipermeable membranes, permit the passage of water and not of sugar. For the sake of clearness, suppose that a solution of sugar be placed in the upper vessel of a diffusion apparatus with a semipermeable membrane, and distilled water in the lower. In this case the molecules of water in the lower vessel can penetrate into the upper, while on the other hand those in the upper cannot escape into the lower. The reason for this is simple; for if water escaped from the sugar solution without an equivalent amount of the sugar, the solution would be more concentrated. Now in order to concentrate the sugar solution, work has to be done; for example, it may be concentrated by heating it. But in the diffusion apparatus there is no source of energy available for concentration, and the result is that the water cannot escape from the upper vessel. On the other hand, the membrane being permeable for water, the molecules in the lower vessel find no difficulty in entering the upper. The result is that the sugar solution becomes more dilute, while the water in the lower vessel diminishes in volume until it may disappear altogether. If sufficient pressure be applied to the sugar solution, the water will cease to enter it from the lower, and the amount of pressure which suffices to arrest the movement of the water is known as the *osmotic pressure* or *osmotic tension* of the sugar solution. The phenomenon is known as osmosis, but it must be recognized that osmosis is merely a diffusion under special circumstances, for the whole is due to the movement of molecules, all of which are free in ordinary diffusion, while some of them (*e.g.*, sugar in the above example) are restricted in their movements in osmosis.

The osmotic pressure is found to vary directly with the number of molecules in the solution, a concentrated solution causing a more rapid flow and a higher pressure than a more dilute one. Thus a one-per-cent. solution of cane sugar exercises a pressure of 535 mm. of mercury, a two-per-cent. of 1,070 mm., and so on. The pressure exercised by even dilute solutions is very considerable, as is seen on transforming these figures into atmospheres, for a two-per-cent. sugar solution is then found to give a pressure of nearly one and a half atmospheres. This is even more remarkable when a smaller molecule than sugar is chosen. Thus a one-per-cent. solution of potassium nitrate exercises a pressure of over three atmospheres. As the pressure depends upon the concentration of the solution, it decreases and the movement becomes slower as the process goes on, for the water diffusing into the sugar solution dilutes it.

As osmosis is merely a special form of diffusion, it follows that only diffusible and dissolved substances can exercise osmotic pressure. The colloids, such as proteids, are therefore generally believed not to have any influence on the movement of fluids because they are not in true solution, but rather in a state of suspension. Others hold that though in solution, they exercise no appreciable tension because the molecule is so large. As each molecule in solution has the same osmotic effect, it stands to reason that a one-per-cent. solution of sugar must induce an immensely greater pressure than a one-per-cent. solution of albumin, because the number of molecules dissolved in the former is so much greater. The proteids always contain a certain amount of soluble salts, and these are sufficient to cause some osmotic tension; so that it is not yet decided which explanation is correct, but in any case the osmotic pressure of the proteids is so small as to be negligible.

Very often membranes are met which offer a certain amount of resistance to the passage of dissolved diffusible bodies while allowing water to pass freely. If such a membrane separated a sugar solution and water, the latter would at first pass through into the solution rapidly under considerable osmotic pressure. But some sugar also passes downward, and there is thus formed a strong solution of sugar above rapidly being diluted and a weak solution of sugar below rapidly becoming stronger from the continued permeation of sugar into it and the escape of water upward. Finally equilibrium is reached by the solutions on each side of the membrane attaining the same concentration.

The same principles hold when solutions are present on each side of the membrane, the direction of flow being always toward that side on which the larger number of molecules are present, provided the membrane is semipermeable. The osmotic pressure is determined by the difference of the osmotic pressures of the two solutions toward distilled water. If the same body is in solution on the two sides of a permeable membrane, the water tends to pass toward the stronger solution, while the solid passes in the opposite direction until equilibrium is reached. When two different bodies in solution, *e.g.*, sugar and urea, are separated by a membrane which is permeable by each of them, they diffuse freely through it and the two solutions soon become identical, each containing the same percentage of urea and sugar. If the urea can penetrate the membrane while the sugar fails to do so, the osmotic pressure is that of the sugar solution and the urea solution will pass toward the sugar as long as the latter can exert appreciable pressure. In other words, no osmotic pressure is exerted by a fluid toward a membrane which it can pass through.

When neither sugar nor urea can pass through the membrane, the water passes from the solution containing the smaller number of molecules toward that containing the larger number until equilibrium is established by each solution containing the same number of molecules per cent. of water. The weaker solution is often known as the *hypotonic* or *hypoisotonic*, the stronger as the *hypertonic* or *hyperisotonic*, while two solutions possessing the same osmotic pressure are known as *isotonic* solutions.

In biology the problems in diffusion are much more complex than the examples given above, but they all depend on these general rules. In the first place the solutions are much more complicated, containing a number of different substances in solution; in the second, the membranes are neither perfectly permeable nor semipermeable. They permit the passage of some of the constituents of the fluids, but as a general rule few of these pass quite freely, and the amount of resistance varies with each kind of molecule. Further it must be recognized that a dissociated salt exercises not the osmotic tension of a

molecule, but that of its ions. In a dilute solution of sodium chloride, for example, the osmotic pressure is not measured by the number of molecules, for each ion exercises the same osmotic effect as a molecule of sugar, or as an undissociated molecule of salt.

Each cell in the body may be conceived as the inner vessel of a diffusion apparatus, separated from the surrounding fluids by a membrane, for though this membrane has no anatomical existence, the colloid nature of protoplasm has the same final effect as if the cell were surrounded by a membrane. All cells are permeable by water, but each kind of cell appears to differ in the facility with which it permits the permeation of salts and the other bodies dissolved in the body fluids. Some, for example, allow the passage of ammonium readily, while others refuse it entrance. Others take up sodium sulphate as readily as sodium chloride, while others accept the latter and reject the former. Now if the intercellular fluid contains any substance which is not capable of penetrating the cells, it must exert osmotic pressure on the cell; and unless this pressure is counterbalanced by other bodies in the interior of the cell which similarly cannot escape from it, the fluid of the cell will be drawn out and shrinkage will result. Every cell in the body then must be conceived as existing in a condition of equilibrium, the osmotic tension of the salts, etc., in its interior being pitted against that of the surrounding fluid, and the smallest change in either of these leading to an inflow or outflow of water from the cell. Now such changes are continually in progress, for as the proteids and carbohydrates of the cells are broken down into simpler bodies, soluble in water, each molecule so formed acquires osmotic properties, and either diffuses freely into the surrounding fluid, or causes an inflow of water into the cell. In either case the equilibrium is disturbed until the new product is removed by the excretory functions. The importance of diffusion and osmosis in the functions of the body cannot therefore be overestimated; in fact, it may be said that while the more obvious movements of the fluids of the body are determined by the circulatory mechanism, the finer but no less important exchange between the cells and the intercellular fluid is in large part directed by the laws of diffusion. And while a knowledge of the arterial supply of an organ is recognized to be necessary for an understanding of its physiology and pathology, it is probably no less desirable to ascertain the permeability of its cells for the constituents of the surrounding fluids. The osmotic pressure varying with the nature of the membrane or cell, and also with the salt in solution, the only way to determine the results of exposing the cell to a solution of the salt is the experimental, and a considerable amount of work has been done in this direction, so that the permeability of some cells is known for a large number of salts and other bodies. In this method of procedure the cells under examination, *e.g.*, the red blood cells, are exposed to solutions of different strengths, and the concentration which induces neither shrinking nor swelling of the cell is ascertained. This concentration is that balanced by the intracellular fluid, and the solution is said to be isotonic for that cell. The salt in solution must obviously fail to penetrate the cell, or do so only extremely slowly, for if it permeates freely the water in which it is dissolved will also pass into the cell and expand it. In such an isotonic solution the number of molecules percent is exactly equal to that in the interior of the cell, and a solution containing the same number of molecules and ions of any other non-permeating salt will also be isotonic and cause no change in the size of the cell. For example, if a 0.75-per-cent. solution of sodium chloride has been found isotonic for the blood cells, an equivalent solution of sodium sulphate or of ammonium chloride will also preserve the size of the cells unchanged, provided these salts are equally incapable of permeating the cell. If one of these, *e.g.*, that of ammonium chloride causes swelling of the cell and the escape of hæmoglobin, then this salt must permeate more freely than sodium chloride.

In the case of non-dissociating bodies, such as alcohol, sugar, or urea, equimolecular isotonic solutions can be made by calculating the atomic weights. In the case of the salts this method fails, for the dissociation varies for different salts and for different dilutions, and each ion exercises the osmotic pressure of a molecule. Other methods have therefore been adopted, and of these the estimation of the depression of the freezing point has come into general use in the last few years. This method, it must be emphasized, does not indicate the osmotic pressure for all membranes, nor the permeating qualities of the substance, but only the total number of molecules and ions in the solution. It depends upon the fact that solutions containing the same total number of ions and molecules per cent. freeze at the same temperature, which is lower than that at which distilled water freezes to ice. If two solutions lower the freezing point an equal extent below 0° C., therefore, they contain the same number of ions and molecules, and are isotonic toward a semi-permeable membrane. The estimations are made by means of thermometers reading to $\frac{1}{100}$° C., and allowing of approximations to $\frac{1}{1000}$° C., and with some care and practice in the method very exact determinations may be made. A very extensive use of this freezing method has been made in experimental work, and some results have also been obtained in clinical medicine, but the details of the method can only be given in works dealing specially with this subject. The depression of the freezing point of any solution below that of pure water is generally expressed by the symbol $\triangle$. If the salt is not capable of penetrating a cell, its osmotic pressure varies with the $\triangle$ of the solution, *i.e.*, with the concentration of molecules and ions, and if two solutions of non-permeating salts have the same $\triangle$, their influence on the movement of the fluid of the cell will be equal. On the other hand, if the salt permeates without difficulty, the $\triangle$ is of no significance in regard to the effects of the solution on the cells.

The relations of the salts to the tissues has been worked out in most detail in the case of the red blood cells. It is found that in a 0.75-per-cent. solution of sodium chloride, the cells maintain their form and size unchanged, *i.e.*, the salt fails to penetrate the cells and exercises the same osmotic pressure as the diffusible contents of the cells, or is isotonic with the fluid in the interior of the cell. If the cells be exposed to pure water, they swell up and discharge their hæmoglobin, and the same occurs in weak (hypotonic) solutions of sodium chloride. The salt here being in lower concentration than the contents of the corpuscles, a current of water sets inward toward the stronger solution. In solutions of greater concentration than 0.75 per cent. (hypertonic solutions) the cells shrink from the loss of water, which flows outward toward the stronger solution. Similar phenomena are seen when other salts of the fixed alkalies are employed, so that these salts appear to be unable to penetrate the corpuscles except to a very slight extent.

In solutions of ammonium chloride, on the other hand, the cells swell up and lose their hæmoglobin, whether the solution be isotonic with 0.75-per-cent. NaCl, or much stronger. The conclusion is that the ammonium chloride can penetrate the cells and thus exercises no osmotic resistance to the entrance of water, so that the effect of ammonium chloride solution is practically identical with that of pure water. Many other ammonium salts resemble the chloride in penetrating the red blood corpuscles; but others, such as the sulphate and phosphate, fail to enter the cell entirely, or penetrate with great difficulty. The sulphate and phosphate ions, therefore, like the sodium and potassium ions, are non-permeating, and exercise osmotic pressure on the cell wall. Unless both ions of a salt can enter the cell, neither does so. Many non-electrolytes, such as urea and compound ammonias, appear to enter the blood cells freely.

The absorption of salt solutions in the intestine also presents an interesting example of the importance of diffusion in vital processes. A solution of sodium chloride isotonic with the blood is absorbed readily, whence it is inferred that sodium chloride can penetrate the mucous membrane. A hypotonic solution is similarly taken up

easily, and still more readily pure water. A hypertonic solution, on the other hand, disappears from the bowel more slowly, and very often the fluid first increases in the lumen until it has become almost isotonic with the blood, and only then disappears into the tissues. The sodium chloride does not, therefore, permeate the bowel wall without resistance, otherwise a hypertonic solution would be taken up as quickly as distilled water. On the contrary, a hypertonic solution first exercises osmotic pressure on the cells and causes them to lose water. At the same time some of the chloride has disappeared into the cells, and the solution remaining is diluted with the water exuding, until it is so weak that the osmotic resistance is overcome by the absorbing forces and the whole is absorbed into the blood.

When the sulphate of sodium passes into the bowel in solution, this feature is still more marked. An isotonic solution has little tendency to be absorbed, and on the other hand is not increased in volume, the solution in the bowel counterbalancing the osmotic pressure of the cell contents. A hypotonic solution decreases slowly because its osmotic pressure is less than that of the cell contents, and water therefore tends to pass from the weaker fluid in the lumen to the stronger in the blood; but the fluid escapes from the bowel much more slowly than in the case of an hypotonic solution of sodium chloride. If hypertonic solutions be used, the bulk is at first much increased owing to fluid from the blood escaping into the stronger solution. Finally the sulphate solution becomes isotonic with the blood and is very slowly absorbed if the weight of the fluid in the bowel does not set up reflex peristalsis and cause evacuation. This slow absorption from the bowel is still more marked in the case of magnesium sulphate, in which both ions appear to be taken up with reluctance by the mucous membrane. As these salts fail to leave the bowel and retain the water in which they are dissolved, they render the contents more fluid than usual, and the unusual weight and distention cause peristaltic movements and evacuation. The purgative action of the saline cathartics arises from the difficulty with which they enter the epithelial cells. It is to be remarked that here, as in the case of the red blood cells, the sulphates diffuse with greater difficulty than the chlorides; on the other hand, the chlorides of the fixed alkalies are taken up freely by the bowel wall, while they fail to permeate into the corpuscles, and the oxalate of ammonium, which penetrates the blood cells, is rejected by the epithelium.

The presence of the salt solution in the stomach and intestine inducing such movements of fluid into the bowel and back into the blood, naturally causes considerable disturbance in the distribution of the fluids of the body. When a strong sulphate solution is diluted by fluid poured into the intestine, for example, this fluid comes from the blood and indirectly from the fluids of the tissues. A similar exchange without doubt follows the absorption of salt solutions into the blood, but this is difficult to follow experimentally. When salt solutions are injected into the blood-vessels, however, it is found that there is a marked disturbance of the equilibrium of the tissues. If the solution is hypertonic, there is a flow from the lymph spaces toward the blood which continues until the plasma recovers its normal density The current then is found flowing in the opposite direction from the blood-vessels into the tissues. The lymph measured in the thoracic duct is found to be lessened at first owing to the inflow into the vessels, but later more lymph passes along the duct than usual, owing to the current of fluid passing toward the tissues from the blood.

The injection of salts into the blood-vessels or their absorption from the bowel leads to considerable diuresis. The explanation of this diuresis is still a matter of discussion, but there can be no question that the diffusion and osmotic properties of the salts play an important rôle in this result. The accumulation of fluid in the blood at the expense of the tissues naturally leads to an unusual bulk of the contents of the blood-vessels, and this in turn to an increased pressure in the capillaries. This engorgement of the vessels cannot be relieved by an outflow into the tissues, for this is prevented by the current of lymph pouring into the vessels. Only one way of escape remains, that through the kidneys, and the inflow of lymph is therefore accompanied and followed by diuresis, which is thus in large part explained by the physical forces, although there is doubtless much still obscure in the process. Different salts vary in their diuretic properties, and this might at first seem to indicate that the diffusion was of secondary importance. As a matter of fact, however, many of these differences can be explained by varying rates of diffusion. For example, the sulphates are as a general rule inferior diuretics when given per os, because they fail to reach the blood for the most part from their cathartic action. On the other hand, sulphate of sodium, injected intravenously, causes much greater diuresis than an equimolecular solution of sodium chloride, even if it causes the same inflow into the vessels and the same degree of hydræmia. This has been explained, however, by the renal tubules failing to absorb the sulphate, while taking up the chloride readily. If this is the case, as appears very probable, the sulphate failing to penetrate the renal tubules and thus return to the blood, must hold a certain amount of water in the tubules which would otherwise return to the blood. The chloride, on the other hand, returns readily through the epithelium lining the tubules, and thus retains less water in the tubules and causes less diuresis In this view the epithelium of the tubules resembles that of the intestine in repelling sulphates and phosphates and admitting chlorides readily, but differs from it in showing little avidity for urea and sugar.

The urine is generally a much more concentrated fluid than the blood; that is, it contains a larger number of molecules and ions. The kidney must thus do a considerable amount of work in concentrating such a fluid from the more dilute blood plasma, and by estimating the Δ of the blood, which is remarkably constant (about -0.56° C.), and comparing it with that of the urine, the actual work done may be estimated exactly. Dreser calculated the work done by the kidney in forming 200 c.c. of average urine at the large sum of 37 metre kilograms, or over 270 foot-pounds, but this may be greatly exceeded in cases of very concentrated urine. Attempts have been made to use this method of estimating the work of the kidney in clinical medicine, and the subject has been treated of at great length in recent years under the title of cryoscopy. As yet no results of importance bearing on diagnosis or prognosis in renal affections have been arrived at.

When very concentrated solutions of salts or other dif fusible bodies are brought in contact with living cells, some fluid escapes from these into the solutions, and this often deranges the activity of the cell. This may be observed in the stomach when strong solutions of such harmless bodies as common salt or sugar are swallowed, the disturbance of the equilibrium manifesting itself in irritation, nausea, and vomiting. In the same way a strong solution applied to wounds or mucous membranes causes irritation and pain from the withdrawal of fluid and precipitation of proteids. The same desiccation of the tissues may arise to a less degree from the presence of excess of salt or sugar in the blood. The organs which suffer chiefly are the brain and spinal cord, as is manifested in tremors and convulsions, and later by paralysis and asphyxia, when strong solutions of salts, sugar, urea, or other diffusible substances are injected intravenously in animals. *Arthur R. Cushny.*

DWARFISM.—Nanosomia or microsomia is a condition, found in both animals and plants, in which the stature and weight fail to reach the normal minimum for individuals of the same species. The word *nanosomia* is derived from two Greek words, *νᾶνος*, a dwarf, and *σῶμα*, a body, the former being the equivalent of the Latin *nanus* or *pumilio*, the Anglo Saxon *dweorg* or *dwerg* and the German *Zwerg*.

From stray references to the subject in the pages of writers of antiquity, we may infer that a belief in the

existence of dwarfs has been general from the most remote times. Homer, Herodotus, and Aristotle, among others, speak of a pigmy race that was to be found near the sources of the Nile. In India, too, there was a current belief in dwarfs descended from Hoonuman, the monkey-god. Many of the statements in regard to dwarfs are, however, so wildly improbable that they were, no doubt, based on mere "sailors' yarns," and are entitled to about the same amount of credence as the famous "Travels" of Sir John Mandeville. That they contain a modicum of truth, nevertheless, is proved by the discovery of diminutive peoples by modern explorers, such as Paul Du Chaillu, Schweinfurth, Battel, and Kolle. Dr. Schweinfurth, for instance, has found in the country to the south of the Nyam-Nyam a race called the Akkas, varying in height from four feet to nearly five, who are probably the same as those referred to by Herodotus. Any exhaustive discussion of the subject of dwarfism from an ethnological point of view would be out of place in a work of this nature, which is more properly concerned with the biological and pathological problems involved, but yet, apart from the interest that always invests the curious, it may not be entirely stale, flat, and unprofitable to possess ourselves of the main facts.

From the golden days of imperial Rome it was the fashionable thing to keep dwarfs. The most famous of these were Conopas and Andromeda, belonging to Julia, the niece of Augustus, each of whom measured only two feet four inches. Many of these dwarfs were, no doubt, the natural article, but the number of these was insufficient to supply the demands of cruel display and luxury; consequently they had to be produced by artificial means. One favorite method was the simple one of depriving children of suitable food. They became rickety, and while many died, those who survived were highly prized. Another plan, in some vogue, was to rub the back with the fat of bats, moles, or dormice. Somewhat similar was the practice of washing the backs and feet of pups, the drying and hardening of the parts resulting from this being supposed to stunt the growth. Even at the present time, it may be remarked, attempts are made to limit the growth of boys intended for jockeys by sweating. The practice of keeping dwarfs persisted through the Middle Ages into the eighteenth century. Lady Mary Wortley Montagu, when in Germany, found the dwarf a necessary appanage of every noble family. She describes the imperial dwarfs at Vienna "as ugly as devils," and, "bedaubed with diamonds." In these days dwarfs were not infrequently noted for their wit and wisdom, and, like the court jesters, whom in fact they superseded, were allowed unlimited freedom. It is said that one of the Danish kings actually made his dwarf prime minister in order to get at truths that other men were afraid to utter. Peter the Great, among other vagaries, was interested in dwarfs, and in 1710 gave a feast to celebrate the marriage of his favorite Valakoff with the dwarf of the Princess Prescovie Feodorovna, at which seventy-two dwarfs of both sexes were present. The practice of keeping dwarfs was widespread, and has been immortalized in the canvases of some of the most celebrated painters, notably Velasquez, Raphael, Paul Veronese, Domenichino, and Mantegna. Their delineations are in some cases of much value in enabling us to determine the nature of the dwarfism known to former times. In fiction, too, the dwarf has played a prominent part, as readers of "Peveril of the Peak" and "The Black Dwarf" will remember.

Some personages, famous in history, have been of small or even diminutive size. Philetas, of Cos, tutor of Ptolemy Philadelphus, was, according to Ælian, so light as well as small that he was obliged to carry leaden weights in his pockets to prevent his being blown away. Others that might be mentioned are Attila the Scourge, Æsop the fabulist, Procopius, Gregory of Tours, Pepin le Bref, Prince Eugene, Admiral Gravina, Fleury and Garry the actors, Arendt the Danish antiquarian. In England the history of dwarfs is traceable to mythological times. The origin of the almost generic title of "Tom Thumb" is to be found in an ancient ballad, which informs us that "In Arthur's court Tom Thumb did live." The most famous English dwarf was Sir Jeffery Hudson, who was born at Oakham in 1619. He made his first appeal to fame when he was presented by the Duchess of Buckingham to Queen Henrietta Maria as he stepped out of a pie. From the age of eight till thirty he was only eighteen inches high, but afterward suddenly shot up to three feet nine. He became a well-known courtier and was entrusted with several matters of delicacy. He did not lack courage for he fought two duels, one with a turkey-cock, celebrated in the verses of Davenant, and another with Mr. Crofts, who came to the meeting with a squirt. A more serious encounter, however, followed, for little Jeffery, who was mounted on horseback to compensate for his inferior height, shot his opponent dead. He was twice made prisoner, once by the Dunkirkers as he was returning from France, and once by the Barbary pirates. On each occasion he was soon ransomed. He eventually, however, fell on evil days, for he was accused of participating in the popish plot and was sent to the Gate House, where he died in 1682.

About the same period, or somewhat earlier, Charles I. had a page at his court called Richard Gibson, who was remarkable for his small size, and was, appropriately enough, a miniature painter. He married Anne Shepherd, the dwarf of Henrietta Maria, the ceremony being performed by Edmund Waller. Together they only measured two inches over seven feet. Evelyn designated Gibson as a "compendium of a man," and the pair were painted hand in hand by Sir Peter Lely. Mistress Gibson had nine children, five of whom survived and were of normal size. She died at the age of eighty, and her husband at seventy-five.

One of the most celebrated dwarfs was a Polish gentleman, Joseph Borwilaski, who became noted throughout Europe as a handsome man, a wit, and something of a scholar. His parents were tall, but three of his brothers were small. He was born in 1739, and died at the advanced age of ninety-eight in the city of Durham, where, by the irony of fate, he is buried by the side of the Falstaffian Stephen Kemble. His height was thirty-nine inches. Diderot wrote a history of the family.

Another remarkable dwarf was Richebourg, a servant and pensioner of the Orléans family, who died in Paris at the age of ninety. He was only twenty-three inches high, and his diminutive size was taken advantage of during the stirring times of the Revolution when, masquerading as an infant in his nurse's arms, he carried despatches in and out of Paris.

Coming to more recent times we may mention Charles Stratton, or "Gen. Tom Thumb," one of the greatest of Barnum's successes. At birth he was above the normal weight of the new-born, but ceased to grow when five months old His height at that time was less than twenty-one inches. He created a sensation in Europe and amassed a large fortune.

Perhaps the next most striking sensation has been the "Lilliputians," a troupe of singers and comedians possessing much talent as burlesquers. They were probably the same individuals who were examined by Joachimsthal in Germany.

Many of the recorded dwarfs have been very diminutive. Buffon mentions dwarfs only twenty-four, twenty-one, and eighteen inches high, and describes one who, when thirty-seven years old, measured sixteen inches, whom he considers to have been the smallest person on record. The "Princess Topaze," a French dwarf, is twenty-three and a half inches tall (or rather short ?), who weighs only fourteen pounds. Her parents were of normal size.

On consideration of the facts recorded in the above remarks we are led to certain important conclusions. Most dwarfs have been well proportioned, without deformity, and of average or more than average intelligence. Some of them have been persons of great vigor and force of character. In fact they may be said to dif-

fer but little from ordinary individuals save in the one point of size.

Dwarfs fall naturally into two classes: Those that are diminutive at birth and subsequently develop slowly, so that they always remain more or less stunted; and those that are of normal or even more than normal size at birth and later cease to grow. Authentic information as to the size of dwarfs at birth is hard to obtain. We may, however, correctly infer that they are often below the average size, for dwarfed mothers have frequently borne children in a natural way, and physical considerations would preclude us from coming to any other conclusion. Conversely, normally developed mothers have not infrequently given birth to dwarf children. Instances are on record of new-born infants weighing a pound and three-quarters, or even less, at full term. The subsequent history, however, of these children is unfortunately often unknown. Home (Philosophical Transactions of the Royal Society of London, 1825) speaks of a child borne by a woman following the Duke of Wellington's baggage train, which weighed at birth only one pound, and measured between seven and eight inches long. At the age of nine it was only twenty-two inches high. This is said to be the same child, called Caroline Crachami, whose skeleton is in the museum of the Royal College of Surgeons near that of O'Byrne, the "Irish Giant."

Inasmuch as in the cases of dwarfism that we have so far been considering the parts are perfect in form and the limbs are in the normal proportion to the trunk, although the body as a whole is defective in size and weight, it has been suggested that here we really have to do with a condition of infantilism which may be defined as a state of imperfect and delayed development, whereby the individual preserves the characteristics of childhood long after these should have disappeared. This view is supported by the fact that in many cases of dwarfism the head is proportionately large, as it is in the infant, the genitalia are undeveloped, and the signs of puberty are absent or delayed. Joachimsthal (*Deutsche med. Woch.*, 1899, xxv., SS. 269–271, 288–290), studying with the Roentgen rays a troupe of exhibiting lilliputians, found that bone formation was imperfect, the various centres of ossification being strictly comparable to those of a child, although the individuals in question were about thirty years of age. Undoubtedly, in some at least of the deficiencies complete development and function may eventually be attained. For instance, many of these dwarfs have proved themselves capable of propagating their kind. One cannot fail to be struck also with the fact that dwarfs frequently reach an advanced age, the reverse of what is found in the case of that other contrasting anomaly of development, gigantism. This suggests certainly not a defect in the vitality of the body as a whole, but rather an anomaly in the nature and direction of the growth. The normal balance between structure and function is upset and the individual may possess the mind and faculties of the adult in the body of the child.

With regard to the etiological factors at work in the production of dwarfism we are compelled to admit that our knowledge is far from complete. Our views therefore must partake largely of the nature of hypotheses. Up to the present time but few cases of dwarfism have been studied, and it is chiefly upon the facts gleaned from these and the results of experimentation that our inferences must be drawn.

The condition of dwarfism is clearly but one aspect of the larger question of dystrophy or dysgenesy. Consequently it can be apprehended only by a reference to the elementary principles governing the formation and growth of tissues.

The developmental forces concerned in the elaboration of a new individual may be inadequate to bring the process to completion. If they are totally inadequate, death of the embryo results. Short of this extreme result, however, the nutritional processes may be so modified that we get a deficiency or excess in growth of the organism, either in part or as a whole, or they may be so perverted that we have actual malformation and deformity. There is, therefore, a close relationship between dwarfism, gigantism, malformations, and monstrous births. The peculiarities of development that result in such anomalies may be inherent in the sperm cell or ovum or both, and in this sense are inherited, or they may be due to causes operating on the ovum subsequently to fertilization, either before (intra-uterine acquired causes) or after birth (post-natal acquired causes). We have, therefore, to take into account primitive peculiarities of cell substance on the one hand, and external causes, nutritional or mechanical, acting on the fruit, on the other.

In this particular certain general considerations are worth noting. Thoma ("Untersuchungen über die Grösse und das Gewicht der anatomischen Bestandtheile des menschlichen Körpers im gesunden und im kranken Zustande," Leipzig, 1882) has called attention to what might be called a general "law of deviation." In adults the normal length of the body is on an average 169 cm. in the male and 163 cm. in the female, while the average weight is 60 kgm. and 56 kgm. respectively. Considerable variations on either side of this norm may occur. Taking a large number of individuals, in one-half the amount of deviation will be anywhere between 0.0 and 3.8 cm. In accordance with the law he has formulated, the fifth multiple of this figure when added to or subtracted from the normal average height will give the outside limit of giant or dwarf growth, and will be reached only once in every thousand cases. According to this an adult would be regarded as a dwarf if the height fell below 163 minus 19 cm., or 144 cm. Similarly 5 kgm. is the approximate aberration in weight from the normal in the adult. The fifth multiple of this, 25 kgm., subtracted from 56, gives 31 as the upper limit in weight for dwarf growth. With regard to weight, we have, of course, to be careful to exclude such conditions as marasmus and loss of height from spinal disease. In the case of the new-born the normal average in length is 50 cm. and the weight 3.2 kgm. The amount of deviation is approximately 1.4 for length and 0.28 for weight. The upper limit for dwarf growth in mature infants at birth would therefore be 43 cm. and 1.8 kgm. respectively. Some allowance for individual peculiarities must be made, for many children that are diminutive at birth make up for the deficiency by rapid growth afterward, while, again, some children that are normal in size and weight at birth subsequently become retarded in their growth and development. This "law," while it gives us convenient data for classification, is, needless to say, very far from being an explanation of the anomaly.

Again, certain adventitious circumstances, acting apparently on the germinal cells, may play a part. It has long been known to stock-raisers that continued in-breeding will result in the production of diminutive offspring. And it is said that after Napoleon's campaigns there was a diminution of from one to two inches in the stature of the French people. This has been attributed to the fact that the strongest and best developed males were drawn for military service, but, no doubt, poverty, famine, and disease, affecting the people as a whole, were important factors. These observations suggest that defective physical development on the part of one or both progenitors may lead to insufficient vitality, or what might be termed "relative vegetative inertia" on the part of the germinal cells. This leads us to the consideration of the importance of heredity in this connection.

The inheritance of a developmental anomaly is well illustrated in the case of polydactylism. This peculiarity has been known to persist for three, four, or even five generations, although it may in time be eradicated by marriage with normal persons. The Foldi family, belonging to the Arabian tribe of Hyabites, all have twenty-four digits. They never marry outside the family, and the anomaly is so constant that any child having the normal number of digits is put to death as the offspring of adultery. Reference will be made later to the influence of pressure of the amniotic sac upon the growing embryo in the production of this and other deformi-

ties, but it would be absurd to suppose that such a cause could be present throughout several generations and in a whole race. We are driven to conclude that there must have been some anomaly in the formation and development of the "Anlage" arising in the earlier stages of embryonic life. This being so, it would not be surprising to find the influence of heredity somewhat marked in the condition of dwarfism. As a matter of fact, dwarfism is not invariably an expression of a hereditary peculiarity, although sporadic cases may occur in several generations derived from the same stock. Certain parents nevertheless seem to have a tendency to produce dwarfs. To cite only one example, the celebrated Borwilaski had a brother and sister who were dwarfed. The fact, however, that while certain members of a family may be dwarfs, others may be normally developed indicates that the cause, whatever it be, is not a constantly acting one, or else that there are a number of factors which must be correlated before the given result will take place. That the issues involved may be very complex is well illustrated by an extraordinary instance related by Ekman ("Dissertatio medica descriptionem et casus aliquot osteomalaciæ sistens," Upsaliæ, 1788) where dwarfism and osteopsathyrosis were associated through three generations. The ancestor could not walk because of deformity. He had four children, of whom one son was a dwarf and one daughter was small and deformed. This son begat by a healthy wife a son who had curved extremities, and was liable to fractures on the slightest provocation. This son in turn married a healthy woman who gave birth to a son who had so many fractures that when he reached adult life he could not move, and a daughter who was dwarfed and also suffered from multiple fractures in childhood. Apparently, then, heredity may manifest itself, not only in the rate and amount of growth, but also in the structure and composition of the tissues. Moreover, these two factors, simple growth and organic formation, are not always correlated, and may even be antagonistic. Numerous exceptions to hereditary transmission, however, occur, for when both parents have been dwarfs, the offspring have frequently proved to be normal in size and proportion. What, however, is an occasional anomaly in the case of civilized peoples is a constant racial characteristic in certain of the African tribes, such as the Akkas and Bushmen. This can hardly be explained on any other assumption than that an acquired peculiarity, due to unfavorable environment, has become transmitted and in time impressed upon a great number of individuals, unless we are prepared to accept the other alternative that all races of mankind were originally much smaller than they are at present, and, owing to natural selection and the growth of civilization, gradually developed into a superior organization, a view that, at all events, is not supported by history or tradition. Heredity probably has the same bearing in dwarfism as it has in the case of other anomalies; no more and no less.

The influence of extraneous circumstances on the vegetative power of the germinal cells is well illustrated by some comparatively recent and most suggestive experiments.

In experimenting with the fertilized eggs of some of the humbler forms of life, Roux showed that if, in the two-cell stage, one of the blastomeres be destroyed, the other will regenerate the missing half and eventually give rise to a complete embryo. Endres, Walter, and Morgan have come to similar conclusions in the case of the frog, with the additional observation that the peculiarity is characteristic of the earliest stages only and may be entirely suppressed. In 1891 Driesch separated, by shaking, the blastomeres of the sea urchin's egg when in the two- and the four-cell stage. Blastomeres thus separated produced in time a complete blastula, and the resulting gastrula was a perfectly formed dwarf of one-half or one-quarter the natural size, as the case might be. Zoja, too, in some remarkable experiments on the medusa was able to produce dwarfs one-sixteenth of the normal size. Morgan has further discovered the important fact that either a half embryo or a complete half sized dwarf will result according to the position of the blastomere. If, after one blastomere is destroyed, the other be allowed to retain its normal position a half embryo is always produced, as Roux had already shown. If, however, the blastomere be inverted, it gives rise either to a half embryo or a whole dwarf. In this connection we might recall certain early experiments of Saint Hilaire, who produced dwarf chickens by shaking the egg in the direction of its long axis. Thus it would appear that a rearrangement of the cell material may restore that equilibrium of the entire ovum necessary for the production of a whole embryo. This extraordinary power is, however, less marked in the higher forms and is ultimately lost. In view of the fact, however, that parthenogenesis, which is a constant occurrence in some of the lower forms of life, is sometimes to be observed even in such a highly organized creature as the hen, and in fact has been advanced by some authorities to explain the development of certain tumors of the human ovary, it is not impossible that anomalies in the segmentation of the ovum in human beings, may, although rarely, give rise to one type of dwarf at least, namely, that dwarfed from birth. Two factors would appear to be necessary: some cause to blight one-half of the ovum in the very earliest stage of its development, and another producing a disturbance of the cell equilibrium. As to what these factors may be, whether developmental, traumatic, or inflammatory, we have absolutely no information. One or two facts may possibly point us in the right direction. Malposition of the fertilized ovum as a whole may be brought about by intratubal and intra-uterine inflammation, instances of this being tubal gestation and placenta prævia. It is not inconceivable, therefore, that endometritis and deciduitis might lead to blighting of a portion of the embryo and disturbance of protoplasmic equilibrium. That a modification of external conditions does have a profound effect on the developing ovum, in some animals at least, we have ample proof. Dareste, by incubating hen's eggs at a temperature more elevated than that usually employed, got early development and dwarf formation. Gerlach and Koch ("Ueber die Produktion von Zwergbildungen im Hühnerei auf experim. Wege," *Biol. Centralbl.*, xxii., 1884) also obtained a retardation of development and dwarf growth by varnishing eggs so as to exclude all but a small amount of air.

The effect of primitive peculiarities inherent in the germinal cells in producing developmental anomalies of the Anlage has already been noted in regard to polydactylism, and it is now pertinent to inquire in how far deficiencies in the formation of those structures more especially concerned in the general maintenance of nutrition, namely, the cardiovascular and nervous systems, and the thyroid gland, are of importance in the production of dwarfism.

If the circulatory apparatus be deficient either in the size and extent of the vessels or in the formation of the chambers and valves of the heart, it is obvious that the circulation of the blood must be inadequate for the needs of the organism, which consequently may be inhibited in its growth. Long ago Virchow pointed out the association of cardiovascular hypoplasia with other developmental defects, such as scanty production of the pubic hair and small size of the genitalia, conditions that may be regarded as manifestations of partial infantilism, if we take the view of Hertoghe, that there is such a thing as partial infantilism ("Die Rolle der Schilddrüse bei Stillstand und Hemmung des Wachstums und der Entwicklung," Spiegelberg, München, 1900). Gilbert and Rathery (*Presse méd.*, May 7th, 1900) have, it may be mentioned, found a moderate grade of dwarfism in some cases of mitral stenosis.

With regard to the influence of the nervous system in the production of dwarf growth the available evidence is not conclusive. The close relationship of the central nervous system to the nutrition of the tissues is of course admitted by everybody, and we are aware how often injuries to certain ganglion cells or nerve trunks are fol-

lowed by atrophy or other degenerative disturbance. It would not be surprising, then, to find that a defective development of the central nervous system might lead to aplasia or hypoplasia in the embryo. Of course the more extensive defects of the central nervous system, as anencephaly and amyelinia, are incompatible with life, and consequently cannot be adduced as conclusive evidence on the subject of dwarfism. As a matter of fact, however, whatever information we possess seems to negative the position that dwarfism is a neurotrophic disorder. For instance, as Cruveilhier has shown, the most extensive hydranencephaly may exist without a trace of defective development in the rest of the body, and Vogt, Klebs, and Aeby have pointed out that in microcephaly the individual as a whole may in other respects be well developed. The most we can say is that certain forms of local hypoplasia may with some probability be referred to central nervous disturbances. The probability is increased when in a child with such a defect the process extends subsequently, as in a case recorded by Emminghaus (*Deutsches Archiv f. klin. Med.*, Bd. ii., S. 96, u. Bd. xii., S. 49), where there was congenital microplasia of one arm followed in the tenth year by a trophoneurosis of the eye and corresponding side of the face.

That the thyroid gland exerts an important and often controlling influence in the processes of nutrition cannot now be denied. In how far athyroidea has to do with dwarfism is still a moot point. The whole question as to the relationship of the thyroid gland to myxœdema, cretinism, and deficient development generally will be dealt with more at length shortly. Suffice it to say here that there is considerable evidence to support the view that there are many minor forms of cretinism in which the most striking and characteristic features are absent, and where the analogies to dwarfism are close. Küster extirpated the thyroid gland in a boy of fourteen, whose growth was thereby arrested so that he always retained the characteristics of a boy of that age. Eiselsberg (*Langenbeck's Archiv*, Bd. xlix., 1895) removed the thyroid in two lambs a week old. At the end of six months they weighed 10 and 14 kgm. respectively, while the controls weighed 35 kgm. The disturbance was general and involved the brain as well as the skeleton. Kappeler also found in a boy of twelve and a half years, who had been deprived of the gland, that he did not grow and developed some of the symptoms of myxœdema. It may well be, therefore, that infantilism, as Brissaud holds ("Leçons sur les maladies nerveuses," Paris, 1895), is simply an attenuated form of cretinism. Additional support is given to this view by the fact that some of the cases have been improved by thyroid feeding. Cases of this kind have been recorded by Wunderlich (*British Med. Journ.*, ii., p. 1420, 1897) and Dukes (*British Med. Journ.*, i., p. 618, 1898). In Wunderlich's case palpation proved the thyroid to be extremely small. In this connection also should be cited an interesting case of Sulzer's (*Deutsche Zeitschrift f. Chirurgie*, 1893) in which a goitrous thyroid was removed from a boy twelve and a half years of age. In five years he was a typical cretin. He then began to improve and in four years had regained the normal condition. It was found that a portion of the gland had been left behind at the operation, and that this portion began to grow some eight years afterward. In the same way the compensatory development of an accessory thyroid has an important bearing on the question of cretinism. These facts afford a probable explanation for such curious cases as that of Sir Jeffery Hudson, who, as we have seen, after remaining eighteen inches high for twenty-two years, suddenly shot up to three feet nine inches. Even if we are prepared to admit that infantilism is due to athyroidea, the identity of infantilism with dwarfism is not beyond cavil. At most can we say that the explanation may hold good for some of the cases. For, as Lorain was the first to point out, instances are met with in which there is no disturbance of the thyroid gland, and the defect in size is not true infantilism, but rather to be attributed to premature epiphyseal ossification.

So far we have been discussing the relationship of defective organization of the "Anlage" of the various systems to the question of general hypoplasia.

We pass on now to the question of intra-uterine malnutrition. In this connection ill health or improper diet affecting the mother or a local anomaly of placentation is the chief factor concerned. The former act by bringing a poor quality of blood to the support of the fœtus, and the latter presents a hindrance to the free interchange that should go on between the maternal and fœtal bloods. The existence of syphilis, tuberculosis, or chronic alcoholism in the mother might be expected to produce its effect upon the offspring, largely in the form of lowered vitality and increased susceptibility to disease. It is suggestive in this connection that the Japanese are in the habit of producing dwarf pups by feeding the mothers with alcohol. Charrin, furthermore, could produce a similar result by the injection of ptomaïns. Yet the children of mothers the subjects of long-standing disease or cachexias are by no means always diminutive or poorly nourished. The vitium shows itself, not so much in immediate anomalies of physical development, as in disordered function and defective reserve power. Much discussion has centred round the question as to whether there is such a thing as fœtal rickets. Rickets generally makes its appearance during the first or second year of life, after the sixth month, and is commonly attributed to insufficient and improper alimentation, although unhygienic surroundings may also play a part. It is not impossible that analogous causes, operating during intra-uterine life, might produce the same effects. Rickets is not hereditary, although congenital influences may play a part. In former times, and indeed to a large extent even in these days, the term "fœtal rickets" has been used in a very loose way to include several affections characterized by imperfect bone formation, such as syphilis, osteogenesis imperfecta, and chondrodystrophia fœtalis, which are now, thanks to recent studies, separated fairly well one from the other. It is now the general consensus of opinion that congenital rickets, in the sense of a rickets that has run its course previous to birth, does not exist. To this, however, we shall return.

In one or two cases the study of dwarf fœtuses has revealed the fact that there is an abnormal relationship between the fœtal placenta and the maternal structures. The chorionic villi were scanty and were composed of thin strands of connective tissue covered by an abnormally thick layer of epithelium, while at the same time the projections of the maternal decidua did not extend through the thickness of the fœtal placenta, as is usually the case. The explanation of this that has been offered is that there was a defective development of the decidua, but this is almost certainly incorrect. Chipman ("Observations on the Placenta of the Rabbit," "Studies from the Royal Victoria Hospital," Montreal, vol. iv., December, 1902) has shown that the more intimate connection between the fœtal and maternal parts is brought about by a process of absorption, the ectodermal cells of the chorionic villi proliferating and invading the openings of the uterine glands and extending along the sheaths of the blood-vessels. The maternal tissues are thus eroded as it were, and are quite passive in the matter. It may well be, then, that such an anomalous development of the placenta is due, not to malnutrition and imperfect cell growth on the part of the mother, but to a primary fault in the growing embryo that evidences itself in an imperfect development of the placenta. Apparently, however, before such an abnormality can result in dwarfing of the fruit it must be quite extensive, for the given result does not always follow. As Langhans has pointed out, a similar peculiarity of placentation occurs in cases of tubal gestation, where the fœtus is usually well developed.

Further, the proper interchange of blood and nutriment through the placenta may be gravely interfered with owing to inflammatory disturbances. Here syphilis plays a leading rôle. As is well known, in syphilis hereditaria tarda there is a delayed development of the bony and muscular systems, so that a young man of twenty

may look like a boy of ten or twelve. With this there is often an infantile condition of the genitalia and the hair on the pubes and other parts is slow in appearing. The characteristic lesion of syphilis in the placenta is endarteritis, which leads to extensive destruction of the vascular area, with degeneration, atrophy, and fibrosis of the region involved. The placental circulation must in such cases be greatly interfered with. In syphilis, however, other factors enter. We have to admit that the presence of so serious a disease in the parent, usually the father, must have a tendency to lessen the vitality of the germ cell, to say nothing of the presence of the germ of the disease (the existence of which on analogy we can hardly deny) in the fertilized ovum, with all that this implies.

Hitherto we have been discussing what might be called *primary* or *essential* dwarfism (microsomia) in which the predominating element is a deficiency in the vegetative energy of the cells. The affected persons are in fact normal individuals save in the one particular of size and weight. Besides this, however, we have to recognize another class of cases that clearly belong to a different category. I refer to instances of *secondary* or *symptomatic* dwarfism. Here, while the height of the body is below the normal, the weight is not so strikingly diminished as in the true dwarfs. The main feature is, however, that in addition to general hypoplasia, there are evidences of pathological changes in the tissues, particularly in the bones, leading to asymmetry, deformities, fractures, or malformations. The defects are structural as well as nutritional. Just at this point it may be remarked that the exact nature of these cases presents one of the most difficult problems in etiology. In former times many cases of congenital dwarfism of this type were put down to syphilis, rickets, or cretinism. It was soon found, however, that there were some important points of distinction between certain of the cases. The typical features of cretinism were not always present, nor did the disease, if rickets, conform to the picture of the ordinary post-natal affection. These considerations have led investigators to recognize several distinct types, which are by some regarded as separate entities. We have, therefore, to consider in this connection rachitis, cretinism, osteopsathyrosis, chondrodystrophia fœtalis, and osteogenesis imperfecta, affections that agree in this that with more or less stunting of the body there are structural modifications of the bones of an obviously pathological nature. The amount of confusion that has involved the subject is sufficiently indicated by the number of names that have been proposed for the condition—fœtal rachitis, pseudorachitism, cretinoid dysplasia, chondritis fœtalis, micromelia chondromalacica, achondroplasia, chondrodystrophia fœtalis. A decided step in advance has been made through the researches of Kaufmann ("Untersuchungen über die sogen. fœtale Rachitis," Berlin, 1892, u. Ziegler's "Beiträge," 1893, xiii., S. 32–64) who introduced the name chondrodystrophia fœtalis. Here the type of dwarfism is micromelic and the lesions are usually symmetrical. The body is plump, the micromelia rhizomelic, the head large, and the hands often show the so-called "trident" deformity. There are, however, notable differences in the length, curvature, and consistence of the bones of the extremities, and in the configuration of the skull. Kaufmann, consequently, recognizes two groups: one, in which there is a distinct cretinoid appearance of the skull and face, namely, a deeply sunken nose, prominent eyelids and lips, thick cheeks, and large mouth; and another, in which the nose is flattened and retracted as a whole. In the former type the bone is of good consistence although somewhat more vascular than normal, while in the latter the bone is soft. No hard-and-fast line can be drawn between the two forms, and Kaufmann regards them as manifestations of the same process, the differences being due to the chronicity and intensity of the process. The retraction of the root of the nose is usually said to be brought about by premature ossification and synostosis of the os tribasilare. The ethmoid is also somewhat shortened, and in some cases may be the only part affected. Klein has observed well-marked craniotabes in some cases. In some, too, there may be beading at the costochondal articulations, and defective development of the pelvis, glenoid, and cotyloid cavities. Lordosis may also be a marked feature, and Regnault (*Bull. et mém. de la Soc. d'Anat.*, 1901, lxxvi., pp. 559–560) has found the vertebræ involved. The disease begins in fœtal life, running its course usually, as it is believed, from the third to the sixth week. As a consequence the bones affected are the base of the skull, the long bones, the ribs, and the pelvis. The bones formed in membrane, those that in late fœtal life are mainly cartilaginous, usually escape. Kaufmann has described three sub-classes in chondrodystrophia: Chondrodystrophia malacica, in which the bone is soft; C. hypoplastica, in which there are evidences of retarded growth; and the C. hyperplastica in which the epiphyseal ends of the long bones are greatly enlarged. The periosteal ossification is normal, so that the bones become plump and thick, although somewhat irregular, but the growth in length is disturbed owing to faulty ossification at the epiphyseal junctures. Ingrowth of the periosteum at the epiphyseal lines may occur. Microscopically the cartilage cells are deficient in growth, being spindle-shaped and irregularly arranged, while the hyaline matrix is more or less soft and homogeneous. It is not improbable, however, although the majority of children thus affected are stillborn, that when the affection is of mild type or arises late on in fœtal life, existence may be prolonged for some time. Parrot has met with an example in a child seven and a half years old, who measured 94 cm. in length. Certain changes in the bones of the hands, notably in the fingers, seem to prove that the disturbances of ossification may go on at a later period than that above indicated. (See Thompson, *Edin. Med. Journ.*, 1892–93, vol. xxxviii., pp. 1109–1113, and Turner, *Practitioner*, 1899, vol. lxiii., pp. 263–277.) Thompson (*loc. cit.*) has met with two instances at the ages of thirty-six and thirty-nine, and others have been described by Osler (Trans. Amer. Cong. Phy. and Surg., 1897, vol. iv., pp. 190–192), Abt (*Archives of Pediatrics*), Cestan, "Nouvelle Iconographie de la Salpêtrière," 1901, xiv., 277–289), Apert (*Ibid.*, pp. 290–298), and Baldwin (*Medical News*, 1890, vol. lvii., pp. 138–141).

The exact relationship of the disease, called by Vrolik and Stilling (*Virch. Archiv*, 1899, cxv., SS. 357–370) osteogenesis imperfecta, to chondrodystrophia, is still *sub judice*. The studies of Stilling, Hildebrandt (*Virch. Archiv*, 1899, clviii., SS. 426–444), and Harbitz (Ziegler's "Beiträge," 1901, xxx., SS. 605–628) go to show that it is a definite intra-uterine process. There is clearly some defect in the process of ossification, for the bones are soft and brittle, with the result that fractures and deformities are common. Microscopical study has shown that the trabeculæ are few in number, irregular, and imperfectly formed. There is no continuous system of trabeculæ with Haversian canals and lamellæ as in normal bone. A point of great interest is the extraordinary manner of ossification of the skull. The calvarium is formed not of continuous bony plates, but of a multitude of small mosaics, sometimes touching one another, but also attached by bridges of periosteum and dura. In a remarkable case described by Stilling, the cranial covering consisted of a membranous sac which contained scattered bony spicules. So far as is known there is no synostosis of the basal synchondrosis in this disease. While the affection has hitherto been found only in the new-born or in very young infants, it is not necessarily fatal, and Harbitz is inclined to think that some cases of dwarfism that have been regarded as examples of fœtal rickets or chondrodystrophia may have been osteogenesis imperfecta. As in chondrodystrophia porosity of the bones occasionally appears to depend on hereditary conditions, and Bircher (Lubarsch u. Ostertag, "Allg. Aetiologie," Wiesbaden, 1896, S. 53) has found osteoporosis in the case of a chondrodystrophic dwarf (*cf.* also the case of Ekmann, referred to above). We are, therefore, not prepared to

believe with Paltauf ("Ueber den Zwergwuchs," Wien, 1891) that the two affections are not related.

To rickets chondrodystrophia bears much resemblance, although there are several differences. In both there is enlargement of the epiphyseal ends of the long bones (chondrodystrophia hyperplastica), the long bones may be curved, the ribs beaded, and there may be spinal and pelvic deformities. In rickets, however, the arms are usually long. Periosteal bone formation is also interfered with. The periosteum is readily stripped off and the underlying bone is softer and more spongy than normal. As the condition heals the bone becomes unusually plump and dense. Basilar synostosis does not occur in rickets. Microscopic study has shown that the epiphyseal zone of proliferation in rickets is thicker than normal, irregular in outline, soft, and very hyperæmic, so much so that Kassowitz believed the lesions to be of inflammatory origin.

The microscopical appearances of the growing ends of the bones in chondrodystrophia are, however, quite different from those in post-natal rickets. No clear evidence of the existence of rickets originating during intra-uterine life is forthcoming, yet there is a parallel between chondrodystrophia and rickets, for, as is well known, post-natal rickets, if severe, results in the stunting of the growth of the affected individual, and cases of extreme dwarfism have been met with. The lesions are characteristic. The skull is large, although the face is relatively small. The fontanels remain open for a prolonged period, and bone in certain regions, especially the occipito-parietal, may be so thin as to give way under the pressure of the finger (craniotabes) The forehead is usually large and square, owing to the formation of flat hyperostoses over the frontal eminences. The sternum projects and the sides of the chest are drawn in (pectus carinatum). The spine is often curved and the extremities become greatly deformed owing to the weight of the body and muscular action. The pelvis is contracted; dentition is delayed and the teeth are small and badly formed. The condition is by many believed to be due to infection or possibly auto-intoxication. This view is supported by the experiments of Morpurgo (*Centralbl. f. Path.*, 1902, xiii., S. 113), who showed that rickety changes in the skeletons of young white rats could be produced by the injection of cultures of a diplococcus. The lesions in rickets, however, are so unlike those of chondrodystrophia in important particulars that it is unlikely that an infective cause is at work in the latter disease. Differentiation between chondrodystrophia and rickets may be made by attention to the following points: The dwarfism in the former is micromelic; in the latter not. Periosteal bone formation is not interfered with in chondrodystrophia, while it is in rickets. In healed rickets the bone is abnormally dense; not so in chondrodystrophia. Basilar synostosis does not occur in rickets. In rickets you do not get "trident deformity" of the hands. Developmental anomalies, like cleft palate and polydactylism, are not found in rickets. Osteogenesis imperfecta is recognized by the fragility of the bones, the peculiar ossification of the cranium, and the lack of basilar synostosis.

It is a suggestive and a striking fact that while we are able to draw these distinctions between the type cases of chondrodystrophia, osteogenesis imperfecta, and rickets, there exist borderland cases in which some of the features of these diseases may be combined. Such a one is that reported by Hektoen ("Anatomical Study of a Short-limbed Dwarf," *Amer. Jour. Med. Scien.*, May, 1903), in which in a micromelic dwarf, forty-five years of age, there were one hundred and seventy-two Wormian bones in the skull, without premature synostosis of the os tribasilare, with shortness and curvatures of the long bones, enlargement of the articular ends, curvatures of the spine, deformity of the pelvis, osteoporosis and multiple fractures, and a fibroid thyroid. A case presenting features both of chondrodystrophia and osteogenesis imperfecta has been described also by the Countess von Geldern-Egmond ("Beitr. zur Casuistik der sogenn. fötalen Rachitis," Inaug.-Diss., Zurich, 1897)

The etiology of these interesting conditions is still largely unknown. Heredity appears to be a factor in some cases. In one case, recorded by Porak ("Beitrag zur Histologie und Funktion der Schilddrüse," Inaug.-Diss., Königsberg, 1892) a dwarf gave birth to one healthy child and a second with all the signs of the so-called "fœtal rickets." Guéniot (*Bull. et mém. de la Soc. Obstet. et gynécol. de Paris*, January, 1893) recounts the operation of Cæsarean section on an achondroplastic dwarf, the child being similarly affected. The parents of chondrodystrophic dwarfs as well as their children are nevertheless often healthy. Heredity seems then to play a minor rôle. The influence of heredity in the case of polydactyly has already been dwelt upon, and it is a curious fact that polydactyly may sometimes be associated with dwarfism. An instance of this will be found in *Hutchinson's Archives of Surgery* for April, 1893, where there is given an illustration of a micromelic polydactylous dwarf, copied from Theodore Kerckring's "Spicilegium Anatomicum," published in 1670. The drawing is not entirely to be relied upon, but it is clear that the limbs were too short for the trunk. Both the hands have seven digits; the right foot has eight and the left nine. The condition is not perfectly symmetrical, for in some cases two of the metacarpal or metatarsal bones are welded together. The long bones are plump, and, so far as it is safe to judge from the imperfect sketch, the ends appear to have been enlarged. The orbits are deformed, the two halves of the lower jaw are already united, and the ribs are short and badly formed. It is clear that here we have an abnormality of development in few respects comparable to rickets. It may be that here, as in simple polydactylism, we are dealing with a primary vitium of development inherent in the germinal cell. This view is supported also by the observation of Kirchberg and Marchand (Ziegler's "Beitr. zur path. Anatomie," Bd. v., 1889), who found cleft palate in a chondrodystrophic infant. One of Bowlby's cases, also, reported as congenital cretinism but really an instance of chondrodystrophia, had a cleft palate and a deformed nose. The right foot had six metatarsal bones but seven toes; the left foot had seven toes.

There is, however, another possible explanation. Recent observations have shown that many forms of hypoplasia, non closure of sutures, and, in fact, the most extreme deformities may result from intra-uterine pressure. The simple weight of a limb resting on a band has been sufficient to erode the soft tissues to the bone. Twisting of the cord about a limb may lead to dwarfing or amputation. The pressure of bands traversing the amniotic sac is also a well-recognized cause of even more extreme deformities, such as anencephaly and craniorachischisis. Dareste believed that a contracted amnion was an important cause of hypoplasia.

In Klebs' text-book of "General Pathology" (vol. ii., 1889, Jena) is an interesting illustration representing a microscopical section through the proliferating end of one of the long bones in a micromelic dwarf. The growing cartilage cells are closely packed together, flattened, with their long axes at right angles to the long axis of the bone. The appearances could not be due to alterations in the ground substance which seemed to be normal, but could be attributed only to the effects of external pressure. This would, of course, lead to inhibited and imperfect ossification. The effects of intra-uterine compression are well illustrated by the experiments of Fol and Warynski (Thèse de Genève), who brought external pressure to bear upon a growing embryo. They found that the head was the part most amenable to pressure, and could to some extent be restrained in its growth. Warynski, also, by exerting pressure at the site of fusion of the two primitive cardiac rudiments, was able to produce a double-hearted monster. Klebs (*loc. cit.*, p. 306) refers to a most remarkable case in which a contracted sac led to a singular malformation. In an ectopic gestation the fœtus was found in a tight sac within the transverse mesocolon. There was syndactylism in the upper extremities and polydactylism in the lower. From the

recorded cases it would appear that contraction of the amnion does not lead to dwarfing of the fœtus as a whole, but that certain parts are more liable to be affected, as the extremities and head. In this connection also may be remembered the fact that hydramnios is apt to be associated with grave deformities, such as exencephaly and spina bifida, and has been found in a case of osteogenesis imperfecta. The effect of intra-uterine pressure has also been emphasized by von Franqué ("Ueber sogenan. fœtale Rachitis," Sitzungsberichte der physicalisch-mediz. Gesellsch., Wurzburg, Jahrg. 1893, S. 80).

It is on the ground of the obvious errors in development which are sometimes associated with chondrodystrophia, and which can only be referred to peculiarities of the Anlage, that Virchow objects to the term chondrodystrophia introduced by Kaufmann. Virchow points out that the condition imperceptibly shades into a pronounced developmental anomaly (*Missbildung*), which is finally represented by the phokomelia of Saint Hilaire.

The small stature, the peculiar facial configuration, and the enfeeblement of mental power, with other minor abnormalities found in some cases of chondrodystrophia, have induced the suspicion that some of these cases of dwarfism are really cases of cretinism. The difficulties in the way of differential diagnosis are great. Thus Dolega, Bernard, and Bircher have pronounced certain cases to be instances of cretinism, and yet a subsequent examination proved them to be Kaufmann's chondrodystrophia, and conversely, Neumann, Scholz, and others have described instances of cretinism as fœtal rickets. The difficulties in the way will be readily comprehended if one considers for a moment the lesions in a typical case of cretinism. In the cretin the stature is almost always stunted, Maffei in twenty-two cases out of twenty-five finding the height to be less than 140 cm., while several were under 95 cm. The limbs and trunk are disproportionate. The head is usually relatively large, the top flat, and the occiput prominent, although microcephaly has been found. The fontanels and sutures remain open for a long time. The root of the nose is retracted, and the organ is short and thick with large wide nostrils. The lips and tongue are enlarged. The teeth appear late and are large. The first dentition usually persists throughout life. There is as a rule no hair on the pubes and in the axillæ. The sexual organs are poorly developed, and puberty, if it occur at all, is late. With regard to the finer structure of the bones in cretins, Langhans (*Virch. Archiv*, 1892, cxxviii.) found that the cartilage cells were small, spindle-shaped, and anomalously arranged, being longitudinal to the axis of the columns. The rows were also often interrupted. The bony trabeculæ were shortened and the marrow spaces in the youngest portions of the bone were large and widely separated. The resemblance to Class I. of Kaufmann's chondrodystrophia is close. Typical cretinism is endemic and associated with goitre. Chondrodystrophic dwarfism is sporadic. Can, then, chondrodystrophia be sporadic cretinism? The recorded cases of chondrodystrophia go to show that the disease is of intra-uterine origin, and so far no evidence is forthcoming to prove that the affection ever arises subsequently to birth. Cretinism is said to be congenital in some cases, but the symptoms usually appear some five to eight months after birth, or even later. It is now believed that the changes in the skeleton of cretins are due to delayed ossification of the cartilages. Hofmeister (*Fortschritte auf dem Gebiete der Roentgen-Strahlen*, Bd. i., Hft. i., 1897), studying a case of cretinism with the *x*-rays, found that the epiphyseal ends of the bones grew slowly, and that the epiphyseal plates persisted for a long time. The bones were small. Ossification may in time be completed, but the process may take years; in fact, cretins may continue to grow until they are thirty or forty years of age. Periosteal osteogenesis is normal, or may be in excess. The peculiar appearance of the nose is due to premature synostosis of the bones at the base of the skull, although, as Niepce, Stahl, and Klebs have shown, this anomaly of bone formation does not always occur.

The stunted growth is believed by Bircher (*loc. cit.*) to be due to defective development of the cartilage cells, as was found occasionally by Virchow and Klebs at the base of the skull. We find, therefore, that cretinism and the so-called chondrodystrophia have much in common. The resemblance can, however, be made out clearly only in the case of chondrodystrophia of Kaufmann's first group. Cretinoid chondrodystrophia might be explained as cretinism that had become marked at a very early period of intra-uterine life.

Further information might be obtained by an inquiry into the condition of the thyroid gland in chondrodystrophia. Hofmeister ("Experimentelle Untersuchungen über die Folgen des Schilddrüsenverlustes," *Beiträge zur klin. Chirurgie*, 1894) holds that the changes in the bones produced by thyroidectomizing rabbits are identical with those found in chondrodystrophia as described by Kaufmann, H. Müller, Kirchberg, and Marchand. Although we must admit the great similarity of the lesions in the two cases, this, of course, does not prove identity. Leblanc (Comptes rend. de Soc. de Biol., 1902, liv., 88–89) states that chondrodystrophia is often associated with myxœdema and that disturbance of the thyroid is the causa morbi. Nasan (*Rév. de Neurologie*, 1901, p. 549) is of the same opinion. There is no need of entering here into the question of the identity of myxœdema and

Case.	Observer.	Type of Disease.	Thyroid.	Reference.
I..	Bowlby	Cretinoid with some signs of myxœdema.	Absent	Trans. Path. Soc., 1884, p. 450.
II..	Kirchberg and Marchand.	Not cretinoid.....	Not enlarged	Ziegler's "Beiträge zur path, Anat.," Bd. 5, 1889.
III..	Dolega	Cretinoid	A few atrophied remains without colloid found.	Ziegler's "Beitr. zur path. Anat.," Bd. 9, 1891.
IV..	Paltauf.....	.....	Very small	"Ueber den Zwergwuchs," Wien, 1891.
V..	His (quoted by Paltauf).	.....	Apparently normal.	
VI..	Bernard.....	Cretinoid.....	Thyroid absent, but a very small accessory found.	"Die Cretine Pohl," Inaug.-Diss. Würzburg, 1892.
VII.–XIX.	Kaufmann	Eight cretinoid	Small in two; without change or at least not enlarged in five.	"Untersuchungen über die sogenannte foetale Rachitis," Berlin, 1892.
XX..	Kaufmann	Not cretinoid; C. hyperplastica.....	Normal	Ziegler's "Beitr.," 1893, xiii., S. 32.
XXI..	Scholz	C. hypoplastica.....	Vascular struma	"Ueber fötale Rachitis," Inaug.-Diss. Göttingen, 1892.
XXII..	Johannessen ..	C. hyperplastica, not cretinoid.....	Normal (microscopical examination).	Ziegler's "Beitr.," Bd. 23, 1895.
XXIII..	Salvetti	C. hypoplastica; cretinoid with some signs of myxœdema.	Hypertrophied	Ziegler's "Beitr.," Bd. 16, 1894, S. 29.
XXIV..	Gaethoff	C. malacica.....	Normal size.....	"Ueber einen Fall von sogen. fötaler Rachitis," Inaug.-Diss., Berlin, 1895.
XXV..	Bircher	.....	Normal size	Lubarsch u. Ostertag's "Allg. Aetiologie," 1896, S. 51.
XXVI.–XXVIII	Leblanc and Regnault.	.....	Normal in all.....	Comptes rend. de Soc. de Biol., 1902, liv., 567.
XXIX..	Hektoen	Mixed type.....	Atrophy and fibrosis; hypophysis enlarged; iodine not determinable in thyroid.	*Amer. Journ. Med. Sciences*, May, 1903.

cretinism, further than to say that it is proved practically beyond doubt that the two are one and the same thing, and due to defect in the function of the thyroid. Any differences are to be explained in respect to the time at which the athyroidea first makes itself manifest. Myxœdema is cretinism manifesting itself in the adult; cretinism is myxœdema of childhood. In opposition to the views of Leblanc and Nasan may be cited the experience of Cestan ("Nouvelle Iconographie de la Salpêtrière," 1901, xiv. 277), who found a condition of chondrodystrophy in a girl nine and a half years old, unimproved by thyroid feeding for nine months, and of Marie (*Presse médicale*, Juillet, 1900, vol. iv.), who in two cases found no benefit from the use of thyroid extract. We should observe, too, that the lesions of chondrodystrophia are said to develop in the earliest period of fœtal life before the thyroid is properly formed.

With regard to the anatomical peculiarities of the thyroid in chondrodystrophia it is not always possible to obtain accurate information. So far as I have been able to trace them they will be found in the preceding table.

Unfortunately, not having access to the original papers in all instances, I am not able to give complete information in the above table, and the number of cases might be added to. We see, however, that out of twenty-nine cases the thyroid is abnormal in eight, either absent, atrophied, or hypertrophied. And it is further striking that in all the cases in which the thyroid is obviously diseased, with one exception, the clinical type has been cretinoid; with, in two cases, some additional features resembling myxœdema. The one exception, Hektoen's case, is probably to be explained on the ground of a compensatory action of the hypophysis, which was considerably enlarged, but otherwise of normal structure. In Bowlby's case, which is recorded as a case of cretinism, being observed before the distinctions between the different forms of abnormal osteogenesis were so closely drawn as they are at present, the skin was œdematous and semitranslucent, the nose was broad and flat, and there were no eyelashes or eyebrows. In Salvetti's case the skin was also œdematous. In the one case in which vascular struma is stated to have been present (Scholz), there were apparently no signs of cretinism; but this anatomical condition of the thyroid does not of course imply deficiency of the secretion; rather is it akin to what is found in exophthalmic goitre or hyperthyroidism. This association of defective thyroid secretion, which must be admitted where the thyroid structure is so extremely altered, with the cretinoid type of Kaufmann's chondrodystrophia can hardly be fortuitous, especially when we note that in the cases that are distinctly without cretinoid features, the thyroid has been, so far as we can judge from the imperfect information that we are given, practically normal. In settling this latter point we can admit as conclusive evidence only cases that have been controlled by post-mortem examination. Still, the position is supported to some extent by clinical cases. It is, it must be remarked, difficult to draw conclusions as to the functional efficacy of the thyroid from an estimate of its size alone derived from palpation. Osler (Trans. Congr. Amer. Phys. and Surg., 1897, vol. iv., pp. 190–192) describes two cases of chondrodystrophia in French-Canadian children, who did not present the cretinoid facies, in whom the thyroid was not enlarged on palpation. Joachimsthal (*Deut. med. Woch.*, 1899, S. 288) also reports a case of chondrodystrophia hyperplastica, without the cretinoid appearance, in which also the thyroid was normal on palpation. As corroborative evidence, also, it may be noted that Virchow (*Virch. Archiv*, 1883, xciv., S. 183), in the canton of Glarus, Switzerland, where goitrous cretinism is endemic, found not a few cases of chondrodystrophic dwarfism without the gross signs of cretinism. It would seem, so far as we can judge from so limited a number of observations, that the cretinoid type of chondrodystrophia, as described, is simply a form of cretinism, or at least due to thyroid inadequacy. If this be the case, it then follows that Kaufmann's chondrodystrophia fœtalis is probably not a distinct disease entity, but that several differing conditions are included under the one name. Some stress has been laid on the peculiar retraction of the root of the nose, which is so evident a feature in typical cretinism, as an aid in the diagnosis of these conditions. It should be said that this feature is not always present in undoubted cretinism and, moreover, the explanation given of it, namely, that it is due to premature synostosis of the os tribasilare, does not invariably hold good. Some of Kaufmann's cases show that retraction of the root of the nose may be present without premature ossification of the os tribasilare. In these exceptions he attributes the appearance to shortening of the bony parts in front of the os. Conversely, the synostosis may take place without producing any effect on the condition of the nose. Consequently too much weight should not be laid on this point.

It would, perhaps, be also premature to conclude that the other forms of chondrodystrophia may not be dependent on thyroid dystrophy. It is true that Cestan, Marie, and Christopher have failed to get benefit from thyroid feeding in chondrodystrophia. As the disease, however, originates during intra-uterine life, by the time the cases come to observation the main damage has been done, and it is not to be expected that any form of medication would have a marked effect on bony structures once they were formed. The only possible chance would be if the cases could be treated from birth; but, so far as I am aware, this has not been done. This fact weakens the therapeutic argument very much. Further, it does not follow that because the thyroid is of normal size and appearance that it is competent to perform its function. While an absolute deficiency in the amount of secretion furnished by the thyroid will undoubtedly produce the symptoms that constitute cretinism or myxœdema, it is quite possible that a relative inadequacy will produce the same symptoms. This aspect of the case, which has been emphasized by Prof. J. G. Adami ("Internal Secretions Considered in their Physiological, Pathological, and Clinical Aspects," Trans. Congr. Amer. Phys. and Surg., vol. iv., 1897) has been constantly overlooked by writers on the subject. The doctrine of internal secretions supposes the existence of some substance, the product of metabolism, for the secretion to act upon. The thyroid, therefore, may be normal, but if the substance upon which it acts is produced in excess, then the gland will be insufficient for its work, and the various symptoms of athyroidea may make their appearance. In some few instances in which the hypophysis has been invaded by a tumor, symptoms of myxœdema have occurred with an intact thyroid, the thyroid and the hypophysis being, as is now well recognized, more or less complementary organs. Relative inadequacy of the thyroid—and, *mutatis mutandis*, the same remark applies to the hypophysis and other glands furnishing an internal secretion—is a factor that can by no means be neglected in these obscure disorders of development. Until, however, we know much more about the nature, chemical and otherwise, of metabolic processes, we must leave such questions to the realm of speculation.

In concluding, we should not forget to say a word or two in regard to the relationship between anomalies in structure and function of the genital tract and the general question of somatic development. It is a matter of common knowledge that the changes in the genital organs which occur at puberty are coincident with an increased nutritional and functional activity of the body as a whole, as is evidenced by the rapid growth, the consolidation of the figure, the production of hair, the deposit of fat, the changes in the voice, and the altered mental characteristics, all of which together constitute the adult type. Certain isolated facts bring this relationship into still greater prominence. Genital hypoplasia, with its associated sexual torpidity, amenorrhœa, and even sterility, has been found in certain dwarfs, in myxœdema and cretinism, in acromegaly, and in some forms of gigantism. This would suggest that there is some

functional relationship between the thyroid gland, the pituitary body, and the genital organs. The almost constant genital insufficiency found in conditions of athyroidea is so well recognized that I need not do more than mention it. That a similar peculiarity may be associated with lesions of the pituitary body is perhaps not so widely known. Some years ago I performed an autopsy on a female about thirty years of age, who died with symptoms of a basal tumor of the brain. The genitalia were markedly infantile in size and appearance. A tumor of the hypophysis was found, although there were no signs of acromegaly. A similar case is one reported by Babinski (Society of Neurology, June 7th, 1900), who found signs of infantilism, viz., lack of body hair, amenorrhœa, an excess of fat, in a girl of seventeen, but without acromegaly, who post mortem exhibited a tumor of the pituitary. Analogous peculiarities have been found in the male in such cases. While it is true that children the subjects of atrophy of the genitals are often small, instances of the reverse are not unknown. Eunuchs are often of more than normal height. The increase in length is most manifest in the lower limbs, a peculiarity that is to be observed also in the capon, or castrated chicken, and in the ox. The relationships suggested by the above observations might be depicted graphically in the diagram (Fig. 5124).

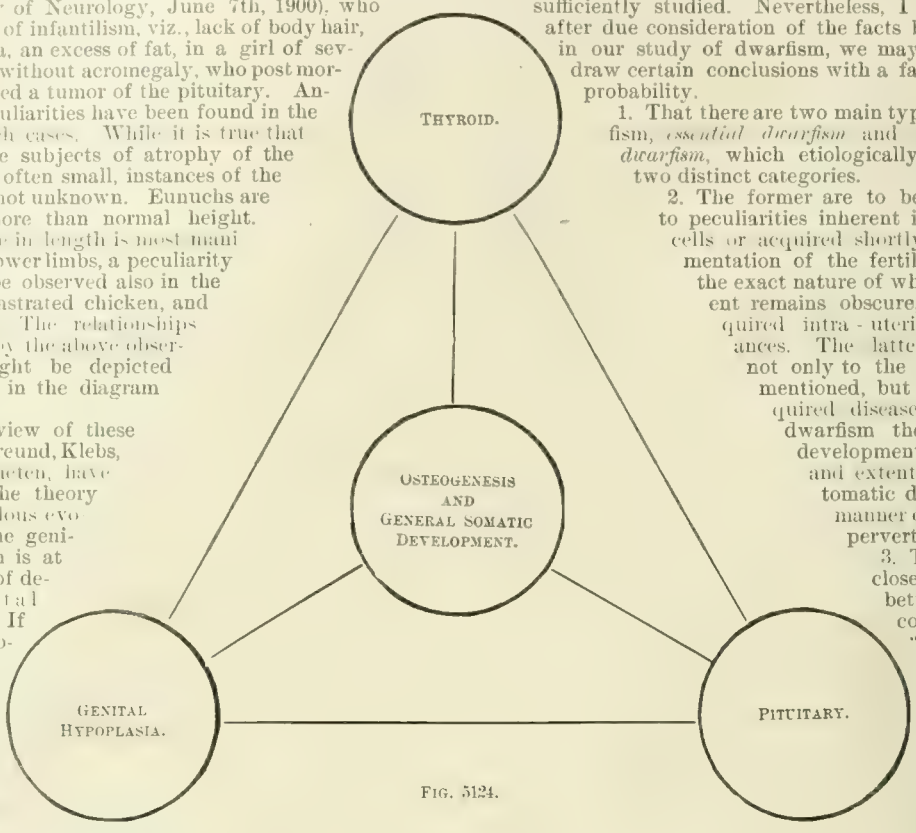

FIG. 5124.

It is in view of these facts that Freund, Klebs, and Verstraeten, have advanced the theory that anomalous evolution of the genital function is at the bottom of developmental dystrophy. If genital evolution be in excess, gigantism or acromegaly will occur; if defective, infantilism or dwarfism results. It seems to me, however, that this is much too strong an assertion, and one that is not supported by the facts, as we know them. Such a theory supposes the existence of an internal secretion in the case of the genital organs, to wit, the testes and ovaries, the evidence for which is not beyond question. Further, the association between genital anomalies and developmental peculiarities is not necessarily direct, as cause and effect, but may be indirect through some third factor. We have experimental evidence to show that defect of the thyroid will produce hypoplasia of the genitalia, but not the converse, and in this case as a matter of fact genital hypoplasia is simply part and parcel of a systemic developmental defect. In the case of the pituitary evidence is scanty, inasmuch as experimentation, except in the single particular of pituitary feeding, is extremely difficult. The evidence, so far as I can gather it from autopsies, seems to favor the view that certain lesions of the pituitary, provided they arise early enough, may prevent the proper development of the genital organs. There is absolutely no evidence to prove that hypoplasia or any other pathological condition of the genitalia has produced disease of the pituitary. Could it do so, one would suppose that, considering the very respectable number of cases of aplasia and hypoplasia of the genital organs that have been described, some abnormality of the pituitary body would occasionally have been noted. This is, however, not the case. It would seem more probable that genital hypoplasia, if not indeed always an effect, is an associated condition merely. In regard to the factors at work in this very interesting but obscure condition of anomalous development, the sum and substance of the whole matter is that our views cannot attain finality until we know much more of the chemistry of the internal secretions and of metabolic processes generally. Hitherto the anatomical peculiarities and the pathological chemistry of the thyroid and pituitary glands in cases of dwarfism and giantism have not been sufficiently studied. Nevertheless, I think that after due consideration of the facts brought out in our study of dwarfism, we may be able to draw certain conclusions with a fair degree of probability.

1. That there are two main types of dwarfism, *essential dwarfism* and *symptomatic dwarfism*, which etiologically belong to two distinct categories.

2. The former are to be attributed to peculiarities inherent in the germ cells or acquired shortly after segmentation of the fertilized ovum, the exact nature of which at present remains obscure, or to acquired intra-uterine disturbances. The latter are due, not only to the causes just mentioned, but also to acquired disease. In true dwarfism the defect of development is in time and extent, in symptomatic dwarfism the manner of growth is perverted as well.

3. There is a close association between such conditions as "fœtal rickets," cretinism, osteopsathyrosis, osteoporosis, osteogenesis imperfecta.

4. Fœtal rickets so called has nothing to do with rickets as it is ordinarily understood.

5. The term *chondrodystrophia fœtalis* is a misnomer, inasmuch as it implies a local lesion, and, moreover, attributes it to a nutritive cause, whereas not only the cartilage but the bone and soft tissues are involved. Virchow is probably correct in regarding it rather as a developmental anomaly.

6. The three types, chondrodystrophia hyperplastica, chondrodystrophia hypoplastica, and chondrodystrophia malacica, are probably not varieties of the same disease.

7. Chondrodystrophia of Kaufmann's first or cretinoid type is probably a modified cretinism.

Albert George Nicholls.

EMBALMING.—This article is intended to furnish useful information to the medical practitioner who may be called upon to preserve a dead body for a limited period of time. This duty can occur only when it is not possible to secure the services of the professional embalmer.

When the object in view is simply to keep the dead human body from undergoing decomposition for a few days, there are a number of methods from which the physician may make a choice. Thus, for example, when it is possible to obtain ice in plenty and the services of a person who can be trusted to renew the supply as fre-

quently as may seem desirable, this method of preventing or at least postponing decomposition is probably as good as any other that can be suggested. But it is often impossible to obtain ice in the desired quantity, or the period of time during which the dead body must be preserved is longer than is compatible with the employment of this method. Under these circumstances it becomes necessary to fall back upon some other procedure, one, for example, which depends for its efficacy upon the employment of chemical reagents. Among the large number of such procedures the physician may be compelled, by reason of the circumstances in which he happens to be placed, to select one of the simpler and less efficacious methods. I will therefore mention a few of these first, reserving to the last an account of the steps which one must take if it be desired to preserve the dead body in good condition for a reasonably long period of time—for months or even years. It is only to such a procedure that the term embalming may with propriety be applied.

Methods Suited to the Preservation of a Dead Body for a Short Period of Time.—(*a*) Place the body, without opening it, and as soon as possible after death, in sawdust mixed with powdered zinc sulphate. The skin, it must be remembered, has a tendency, under continued exposure to this reagent, to assume a yellow color.

(*b*) Open and clean the body and viscera, and keep all the parts that can be reached saturated with a corrosive sublimate solution (1 in 1,000) or a formalin mixture (of a strength of from five to ten per cent.). Cloths saturated with the same fluid should be wrapped around the body, and enough of the preservative should be added from time to time to keep the cloths constantly moist.

(*c*) Open a femoral artery at the apex of Scarpa's triangle and inject a solution of arsenous acid (eight drachms in 9 kgm. of alcohol; cinnabar, q. s.). Then open the abdominal cavity, wash out the cavities of the stomach, bladder, and intestines, and inject the preservative solution into them freely.

(*d*) Camphor dissolved in alcohol, in the proportion of 1 part of the former to 6 of the latter, can be used effectively as a preservative fluid. Another mixture is the following: Oil of turpentine, 5 pints; Venice turpentine, 1 pint; oil of lavender, 2 ounces; oil of rosemary, 2 ounces; vermilion, q. s.

Another mixture, which has been used with some measure of success in England, is the following:—To one pint and a half of glycerin add three quarters of a pound of white arsenic (arsenous acid) and boil; afterward add one gallon of pure glycerin. Still another useful mixture is one composed of alcohol and glycerin in equal parts (each representing forty-seven and a half per cent. of the entire bulk), and carbolic acid to the extent of five per cent. A small quantity of arsenic (about one per cent.) may, if desired, be added to the mixture.

All of the ingredients mentioned in the preceding paragraphs are, as a rule, easily obtainable, and the manipulations required call for no special skill. At the same time it must be remembered that these procedures can at best retard decomposition for only a relatively short time. Thoroughly satisfactory results can be obtained only through the more elaborate and painstaking methods adopted by the professional embalmer.

An Effective Method of Embalming.—Mr. Frank E. Campbell, of 241 West Twenty-third Street, New York City, a recognized authority in embalming, has very kindly allowed the use of the following description of the method of embalming which he prefers:

"I. Bathe and dress (in underclothing) the body to be embalmed, and place it upon a board supported in an inclined position. Close the mouth and eyes, and securely plug all orifices.

"II. Place within easy reach all the instruments and various objects that will be needed, viz., scalpel, aneurism needle, blunt hook, scissors, arterial tube, five six inch lengths of linen thread for tying about the vein and artery when raised, a threaded needle suitable for sewing up incisions, a bulb syringe, a large bottle filled with the embalming fluid, a sponge, a supply of cotton, etc. Sink the suction end of the tubing of the bulb syringe into the embalming fluid contained in the bottle and squeeze the bulb several times in order both to fill it with the fluid and to force out the air which it contains. When these objects have been accomplished the discharge end of the syringe should also be introduced into the bottle, in order that no leaking may take place.

"III. Connect the aspirating pump, by means of tubing and a gooseneck, with an empty aspirating bottle suitable for holding the blood to be withdrawn from the body. Then attach to the free end of the tubing a long silk-covered vein tube, or, better still, a flexible wire catheter.

"IV. Expose the femoral vessels in Scarpa's triangle over an area two or three inches in length and dissect them clean. Then, with one of the lengths of thread already prepared, tie the artery at the lowest possible point with a firm knot, for the injection is to be made only in an upward direction.

"V. Next, pick up the vein and treat it in the same manner as the artery, remembering, however, that the structure of the vein is fragile and that it may easily be punctured or torn. Make a slit, about a quarter of an inch long, lengthwise in the vein. As blood will escape from the vessel when it is thus opened, it is well to prevent this by making pressure upon the vein with the finger or with a blunt hook. Insert the vein tube into the opening in the vein and push it upward to or near the right auricle of the heart. Pass a piece of the thread snugly, but not too tightly, around both vein and tube, and tie it with a simple knot. Attach the tubing of the aspirating pump and begin to pump the air from the bottle. When the air has been withdrawn from the bottle, the vacuum will draw the blood from the body by way of the vein tube. If no blood flows into the bottle after the air is pumped out, it may be assumed that a clot of blood has probably entered the free end of the tube in the vein, or else that there was no blood at the point where the end of the tube rested. Draw the tube slowly downward, and, if there is still no flow of blood, push the tube as far back into the vein as it will go, detach the rubber tubing from it, and, by means of the bulb syringe, inject a bulbful of aqua ammoniæ, for the purpose of dissolving the clotted blood. After this has been done, resume the operation of aspirating. When all the blood that can possibly be removed in this manner has been aspirated, withdraw the tube for about one-third its length, and let it remain in the vein. (Always keep a vacuum in the bottle.)

"VI. Next, pick up the artery, slit it, and insert the arterial tube with care. Then pass the remaining piece of thread around it as far up as you can, and tie it with a simple knot. Attach the bulb syringe (previously made ready) to the tube and begin the injection slowly. When about one-third of a quart of the preservative fluid has been injected, stop and begin once more to aspirate the vein, for by this time the fluid injected into the artery is forcing the blood ahead of it, and the blood will flow again more freely.

"VII. Administer the injections and the aspirations in alternation until a quantity of the preservative fluid varying from three pints to five or six pints, according to the size of the body, shall have been injected, and also until a clear fluid, and not a bloody one, escapes from the vein tube as a result of the aspiration. Any discolorations of the face, ears, or neck, will probably by this time have disappeared. If it should be found, however, that a slight discoloration still remains in the lower part of the ears, or in the neck, a slight rubbing will in most cases remove it.

"VIII. After it is seen that only clear fluid flows into the blood bottle, draw out the vein tube and tie the vein tightly.

"IX. Continue the injection of fluid into the artery until the veins of the temple, the large vein on the forehead, and the jugular vein, as well as the veins in the arms and hands, indicate that they are filled. Then re-

move the arterial tube and tie the artery tightly with the same thread that held the tube in place. Pack the wound well with moist 'lintine,' and sew up the incision with the 'baseball' stitch, drawing the edges snugly together.

"The arterial work is now completed.

"X. For successful work on the cavities of the body there will be needed a twelve-inch trocar, an instrument that will reach every point where it is desirable to apply the preservative fluid. At the same time it must be remembered that much damage can be done with a trocar of these proportions if it be not used with care. It is therefore important to avoid injuring the trunks of arteries and veins, and the various organs.

"Insert the trocar just far enough to penetrate the abdominal wall, and connect it with the aspirating pump. Draw the gases and liquids through it into the empty bottles. Through his knowledge of the anatomical relations of the different organs the physician should be able, without removing the trocar from the opening in the abdominal wall, to carry out successfully the following procedures: He should puncture the stomach and draw from it all the gases and liquid contents, and then, after he has accomplished this, and without removing the trocar, he should inject two bulbfuls of the embalming fluid into the cavity of this organ. The aspirator should then be re-attached to the trocar and the latter should be made to pierce the intestines, both the large and the small. In this way it will be possible to remove any gases or fluids which these organs may contain. The bladder should be treated in the same manner. Never puncture the liver, as it cannot be aspirated or injected, and the original arterial injection may be trusted to preserve it from decomposition. As a final step connect the trocar with the syringe and copiously flood the intestines with the preservative fluid.

"Where death occurs from pulmonary tuberculosis or from pneumonia, turn the point of the trocar upward toward the lungs and cause it to penetrate into the thoracic cavity as far as it will reach. Aspirate first from one pleural cavity—for example, the right—and then from the other; care being taken, after the aspiration of the first pleural cavity, to withdraw the trocar well into the abdominal cavity before the attempt is made to push it on into the second. When both pleural cavities have been thoroughly aspirated, flood each of them with embalming fluid in a cautious manner and then withdraw the trocar altogether.

"With needle and thread close the opening in the abdomen by means of a drawstring suture. Pack the nose with lintine thoroughly moistened with embalming fluid, and pack the rectum and vagina in the same manner. The embalming will then be completed."

While Mr. Campbell does not state which particular preservative mixture he considers the best, it is fair to assume that sufficiently good results may be obtained by the employment of any one of the half-dozen or more standard embalming fluids which are offered for sale in the shops. *William Sohier Bryant.*

EMPHYSEMA, SUBCUTANEOUS.—By this term, or pneumatosis, is meant the presence of air or other gaseous compounds beneath the skin.

The resultant SYMPTOMS are these: a swelling covered with skin of either normal appearance or, if the pressure upon it be great, rather pale; this tumor pits upon pressure, as in the case of anasarca, but the pitting more quickly disappears when the swelling is due to the presence of air. Palpation causes a peculiar crackling or crepitation in the subcutaneous tissues. If the air have entered from without, a wound or puncture can generally be discovered; if from within, expiratory efforts with closed lips and nostrils will generally produce immediate increase in size. It is possible for the whole subcutaneous tissue to become inflated from any superficial part of the body as a starting-point.

In case the emphysema is that of decomposition, there may be an altered hue of the integument; but the discoloration, of course, is entirely independent of the emphysema.

Subcutaneous emphysema may result from causes either traumatic or pathological. Among instances of the latter may be mentioned ulcers or abscesses communicating with the air passages, and, as already suggested, gangrene.

We may include in the discussion of this subject emphysema of other parts external to the lungs, such as mediastinal and submucous collections of air.

In the *head*, orbital emphysema sometimes follows a blow of sufficient violence to break one of the thin and fragile bones of the inner wall of the orbit—the lachrymal or the orbital plate of the ethmoid. If, soon thereafter, the patient blows his nose, the compressed air finds a ready exit from the nose into the orbit, and distends the lids.

Eustachian emphysema: here an ulcer of the tube, or a rupture following awkward Eustachian catheterization, has led to distention and approximation of the pharyngeal walls by the dissecting air. Blowing the nose and the Valsalvian experiment increase the emphysema in these cases. Von Tröltsch[1] mentions a case, within his own experience, in which dysphagia consequent upon such emphysema persisted for five days.

In the *neck* we may have escape of air as a result of foreign bodies, ulcers, or abscesses perforating the œsophageal, laryngeal, or tracheal wall; but emphysema will not be produced if, as a result of the perforation, a broncho-œsophageal fistula be established.

Ulcers of the larynx or trachea may lead to submucous dissection by air. Wounds of the neck penetrating these parts may be followed by subcutaneous emphysema if there is not free escape for the expired air. Under these circumstances inflation of the skin has been known to occur over an area extending from the head to the scrotum.[2]

As a rule, the consequences are not serious; but Holmes[3] quotes Hilton as stating that emphysema about the phrenic nerves may so interfere with their functional integrity as to cause death.

During tracheotomy, and afterward if much inspiratory difficulty be present, Champneys[4] finds that anterior mediastinal emphysema, and even pneumothorax, are liable to occur; and this is especially so if artificial respiration by Schultze's method be employed.

In the *chest* we may have the surgical symptom in question produced in several ways. Pathologically, as by the opening of a vomica or abscess of the lung into the parietes of the chest, the two pleural surfaces being adherent at the point where the abscess perforates. (If the parts were not adherent at this point, there would, of course, simply be a peumo- or a pyopneumothorax.) Emphysema sometimes complicates wounds of the chest-wall, both the penetrating and the non-penetrating varieties. In the latter instance, the air which enters the wound from without during one movement of respiration is prevented in a valvular way from escaping during the opposed movement, and is disseminated by the muscular and tegumentary pressure upon it during this movement. In the case of wounds penetrating the parietal pleura only, we may, besides the consequent pneumothorax, have a subcutaneous emphysema from the same reason.

Wounds that penetrate the lung, and a puncture of the lung by a fractured rib, are alike liable to produce emphysema, air escaping from the lung with the same result as in the case last given.

An additional and rare variety of traumatic emphysema of thoracic origin is that consequent upon rupture of air cells by violent expiratory efforts, with a closed or partially closed glottis, as while coughing, straining, or blowing a wind instrument. Here the air makes its way between the lobules, and, unless it ruptures the pleura, producing pneumothorax, it escapes at the root of the lung into the mediastina, and thence into the cellular tissue of the neck, becoming subcutaneous.

Guttman[5] says: "Most of the cases of this variety of emphysema are observed in connection with croup, diph-

theritis of the larynx, whooping-cough, and bronchitis in children, and with advanced pulmonary emphysema in the aged."

In 1884 I met with the only case which, as yet, I have found complicating whooping-cough. The patient, a child of two years, had been suffering for about three weeks, the parents said, from violent fits of coughing. I was called to treat the sudden appearance of "dropsy" in the case. I found the skin of the head, neck, and chest distended, crepitation everywhere well marked, and no dropsy. Whenever the child coughed the swelling increased in size suddenly, apparently causing distention first in the left supraclavicular region. The respiration was rapid, but seemingly free; the pulse rapid and feeble. The child died within a few hours. Unfortunately, no autopsy was allowed.

In the *abdomen* we may have subcutaneous emphysema from ulcerative perforation of the stomach or intestine at a point previously adherent to the abdominal wall. Unless such adhesions prevent it, gas will escape from the viscera into the peritoneal cavity.

Treatment.—As a rule, air beneath the skin is of slight consequence and requires no treatment, becoming absorbed after a time. If, however, important parts—as the phrenic nerves, or the larynx, trachea, etc.—are subjected to a degree of pressure injurious to respiration, or if the subcutaneous air is spreading further and further, we may employ pressure at the point of escape, or may make incisions through the skin to give relief to tension, or both.

Subcutaneous emphysema possesses an interest for us outside of its pathological or accidental causation. It has often been induced intentionally by the malingerer; and, moreover, its production has been seriously advocated by Dr. H. R. Sylvester[6] in an article entitled "On Life-saving from Drowning, by Self-inflation." Here it is recommended that those in peril of the deep shall make a small puncture or cut in the cheek, leading *from* the mucous membrane about opposite the first molar *to*—but not through—the superficial fascia and skin; and then, closing the lips tightly, they shall proceed to blow themselves up, until the skin of the head, neck, and chest is distended. Dr. Sylvester alleges that a moderate and quite painless and harmless inflation is ample to keep one afloat without effort.

It seems probable that Vidocq refers to such a practice when, in his memoirs—as mentioned by Gavin,[7]—he asserts that he could make his head swell like a bushel, without giving pain, and that he could remove all traces of it by the day following.

In order to test the degree of pain, and the subjective effects of such distention upon the skin, I some time ago performed the following experiment, assisted by my friend Dr. F. A. Manning: Having connected, by a piece of rubber tubing, a hypodermic needle with my compressed-air receiver, I forced air beneath the skin of my left forearm until the limb was much increased in size, the skin tense, and emphysematous crepitation could be felt from wrist to armpit. The pain was very trifling in amount. The distended skin was somewhat anæsthetic; whereas before the injection I could distinguish separate points on the anterior surface at an average distance of 4 mm., immediately thereafter I could name them only when they were 10–15 mm. apart. Still, pinching and pricking were distinctly painful. The emphysema thus induced was slow in disappearing. It was still somewhat noticeable on the third day after the experiment.

As regards the production of emphysema upon the human subject with intent to deceive, it has been employed to simulate hernia, hydrocele, hydrocephalus, ascites, etc. Gavin (*op. cit.*, p. 389) says: "It is a trick used every day by butchers, and has been known from time immemorial by the Ethiopians and mendicants of Abyssinia." Beck[8] quotes Sauvage's "Nosology" regarding a mendicant who "gave his child all the appearances of hydrocephalus by blowing air under the tegument of the head near the vertex." He also cites a case of emphysema of the abdominal parietes, induced by a woman who wished to feign dropsy.

Sir George Ballingall[9] declares that the artificial production of this for the simulation of other diseases is regulated by a recipe current in the British army.

The differential diagnosis of the tumors so caused presents no difficulty. *Robert H. M. Dunbar.*

[1] Treatise on the Diseases of the Ear.
[2] Plaies du larynx, de la trachée, etc., par le Dr. Paul Heurteloup, Paris, pp. 53–77.
[3] Surgery, vol. ii.
[4] Med. Chir. Transactions, 1882, p. 75 *et seq.*
[5] Handbook of Physical Diagnosis, p. 27.
[6] London Lancet, January 3d, 1885, and August 29th, 1885.
[7] Gavin on Feigned Diseases.
[8] Medical Jurisprudence, vol. i., p. 74.
[9] Military Surgery, p. 584.

ENTEROPTOSIS.—(Synonyms: Glénard's Disease, Splanchnoptosis [Stiller].)

Introductory and Historical.—Anomalous downward displacements of the abdominal viscera were described by Virchow, Leube, and others, several years before Glénard's monograph appeared. In this article, which was published in 1885, Glénard set forth his views upon enteroptosis and connected therewith certain nervous phenomena which have since borne the name of "Glénard's disease." Prominent among the features of this symptom complex, which Treves is pleased to call "that medley of symptoms," are downward displacement of the stomach, a movable right kidney, various digestive disturbances, and often very typical neurasthenic symptoms.

The interest thus awakened in postural anomalies of abdominal organs by Glénard's article is as keen to-day as it was eighteen years ago, and many physicians have verified the statement of that author which he made with such enthusiastic earnestness at the close of his early monograph. "I can affirm," wrote Glénard, "that the physician who will follow my directions and strive to verify my statements in such cases will find in his practice the satisfaction which a positive diagnosis gives to both physician and patient, from which alone a proper prognosis can be made, and that satisfaction, the greatest of all, which directs the treatment and avoids for the patient the trial upon him of so many remedies, while at the same time it secures him relief and prevents the physician himself from falling into therapeutic scepticism."

The investigations made by the French were rapidly followed by similar work among the German clinicians, with the result that another view of the cause of the displacements was advanced. Then the English and American writers contributed articles and case reports upon the subject, dealing with the nature and anatomy as well as with the etiology and treatment of the disease. One cannot close this introductory historic note without mentioning the fact that the lectures of Arthur Keith on the nature and anatomy of Glénard's disease comprise one of the best studies upon this phase of the question yet published and will be duly recognized later in this article.

The application of the term Enteroptosis.—It would appear that Glénard's original article included a description of a displacement of the intestines alone. The Germans broadened the application of the term and made it to include, in most instances at least, ptosis of all the abdominal viscera. Schwerdt, however, pleaded that the term was applicable when at least two of these organs suffered downward dislocation. If, on the other hand, one would wish to be specific, the organs so displaced might be specified by *gastroptosis*, for instance, or *nephroptosis*, and so on.

Etiology.—The study of visceral ptosis, from the etiologic standpoint, has provoked a variety of theories differing so widely that it is manifestly impossible to find one theory broad enough to explain all cases. It has been urged that enteroptosis is a congenital anomaly (Stiller); that it is a constitutional ailment (Schwerdt), a general atony of nervous system and muscles; that it is the result of wearing corsets, or tight waistbands with heavy skirts (Meinert); that it is a result of a neurasthenia basis (Charcot); that rapid emaciation or a severe illness

may account for it; that to overlifting or frequent pregnancies many cases may be traced; that adhesions, the result of peritoneal inflammation, may pull down one organ after another (Treves); that it is a reversion to a fœtal or an embryonic type (Rosengart); and the latest, and by no means the least ably supported theory, is that which would regard enteroptosis as "a result of a vitiated method of respiration," and assign it to a place among respiratory diseases (Arthur Keith).

It is admitted, we believe, that there are several factors which maintain the various abdominal organs in position, and of these the most important are: (1) The intra-abdominal pressure, and (2) the ligamentous attachments of the viscera to the body walls. These two are so important that when either fails ptosis may result. Hence it may be said that these factors are those by which the normal postural relations of the viscera are maintained. It is not difficult then to believe that any cause, or number of causes, which lowers the intra-abdominal pressure by exhausting the muscular tone, or which weakens or stretches the supporting ligaments, would readily alter the relation of the organs—especially of the heaviest organs or of those with weakest supports—and result in ptosis.

Thus, as one reviews the various etiologic factors suggested above, one finds most of them—perchance all of them—applicable to a large number of cases. The last theory suggested, however, "enteroptosis as a result of a vitiated method of respiration," certainly requires some explanation. When Dr. A. Keith remarks that enteroptosis is a result of a vitiated method of respiration, he means, doubtless, that faulty movements of the diaphragm, resulting from a variety of causes, determine visceral ptosis, and that whereas under normal relations of the muscles of inspiration—the diaphragm, the external intercostals, and the interchondrals—to the muscles of expiration, and chiefly those of the abdominal walls, there is but slight downward displacement of the viscera. The organs swing and move upon each other, often as much forward as downward, maintaining their normal positions and postural relations. As a result of various conditions the inspiration muscles may "gain the upper hand and the muscles of expiration yield," and ptosis is induced. This writer strongly emphasizes the importance of the diaphragm in bringing about the changes incident to enteroptosis. He remarks that the inspiratory downward displacement, if once the diaphragmatic supports commence to yield, is one of the factors in the causation of visceral ptosis; and while minimizing the function of visceral bonds in the causation or prevention of enteroptosis, he maintains that the active contraction of the crura is the most important factor in the production of visceral ptosis, acknowledging in the same article that while the supports of the diaphragm are threefold—abdominal, costal, and thoracic—doubtless that derived from the abdominal muscles, the muscles of expiration, is of the most importance.

At all events, one is justified in ascribing highest importance to the action of these muscles, since it appears that the normal respiratory swing of the organs, the stomach, liver, and spleen, gives place to downward displacement in the presence of relaxation of the abdominal support, or what is even worse, perhaps, when the body cavity is constricted by corsets or distorted by disease, the action of the diaphragm pushes the organs down. Corsets when applied prevent an inspiratory downward displacement of the liver, but when removed the relaxed condition of the muscles—being too weak to oppose the dropping—favors ptosis.

"The condition essential to the displacement of either kidney is a diminution of the subdiaphragmatic space which may be accounted for, (1) by compression of the thorax with clothing, (2) by a partial collapse of the thoracic walls, following chest or spinal disease, and (3) by the permanent contraction of the diaphragm, which follows a relaxed or paretic condition of the abdominal walls." The left kidney is not displaced so frequently as the right, from the fact that "the left hypochondrium is provided with a safety valve in the shape of the splenic flexure of the colon." So that when the subdiaphragmatic space is lessened, the "colon is extruded and the other organs are left undisturbed." Again, the close attachments of kidney to spleen, and of spleen to diaphragm, prevent dislocation. From the domain of comparative anatomy one may gather some clew also to this condition. It is affirmed that with the evolution of the orthograde posture and the orthograde type of respiration, mesenteric adhesions, which appeared one after the other in five different areas, spread out and bound the alimentary tract more and more to the abdominal wall as the animal became more and more orthograde in posture. Hence, various degrees of extent and strength of mesenteric adhesions due to arrest of development or otherwise, may help to account for visceral ptosis, in some instances at least.

Whatever the active causes may be which bring about enteroptosis, it may be said that the intra-abdominal pressure is lowered, the organs may be pulled down, and there is more than a mere probability that a congenital predisposition exists in the character of the supporting tissues of the organs, whether these be ligaments or muscles, or both.

Clinical Features.

Symptoms.—Enteroptosis does not invariably give rise to symptoms, or, in other words, a considerable degree of downward displacement of one or more of the abdominal organs may exist without calling forth any complaints. On the other hand, however, whether as a result or not cannot always be established, one finds a variety of symptoms referable to the digestive tract, the nervous system, the condition of the blood, and so on; in a word, all manner of subjective symptoms may exist, from the severest abdominal pain, usually spasmodic, to the mildest paræsthesia.

It must be admitted, however, that, prominent and more frequent among the complaints urged by the subjects of enteroptosis, are those of digestive disturbances—distressful weight after food, referred to the right upper quadrant; sometimes spasmodic pain; sometimes vomiting, flatulence, constipation, and throbbing in the abdomen. The distress, which in pronounced cases is for the most part constant and referred to the upper quad-

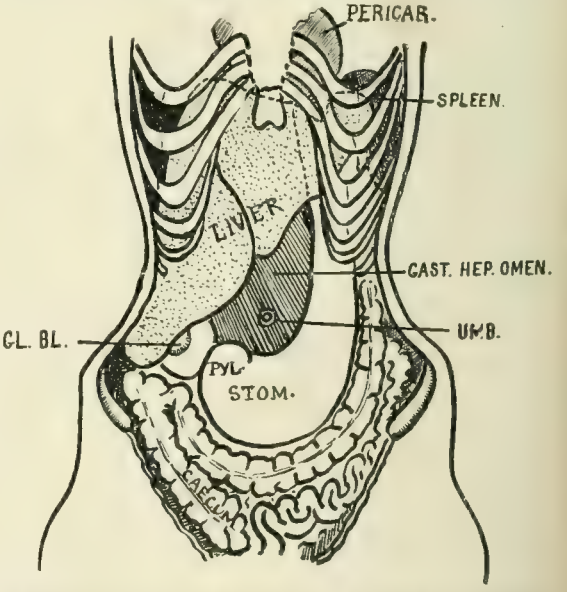

Fig. 5125.—Partial Ptosis of the Viscera in a Woman Aged Forty-five Years. The duodenum descended as far as the brim of the pelvis. (Keith.)

rants, is promptly relieved on assuming the horizontal position, only to return again on getting up and walking about. Hence some persons make this complaint prominent while speaking of their symptoms. It is interesting, in this connection, to note that constipation, which in one case under the writer's observation was very obstinate, at different periods always disappeared when the patient lay in bed for a few days.

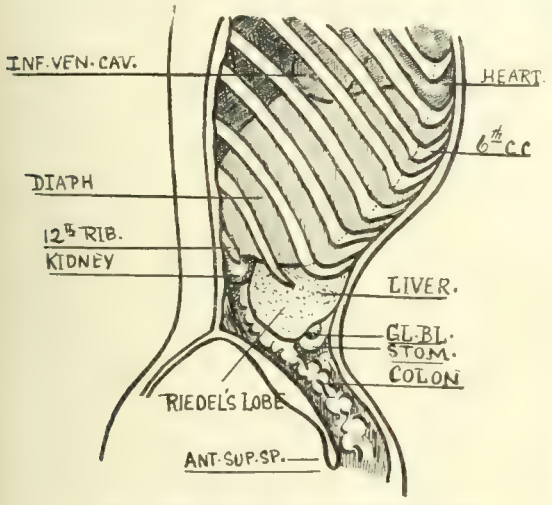

FIG. 5126.—Lateral View of the Same Subject. (Keith.)

It has been seen that the subjects of enteroptosis are mostly women. Those in whom the condition is marked

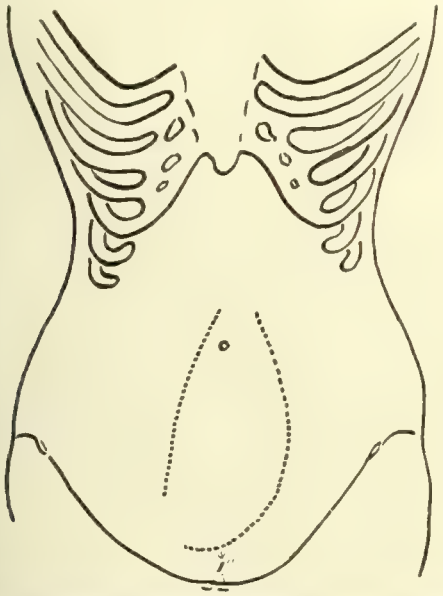

FIG. 5127.—Stomach Vertically Situated and Prolapsed. Located by illumination.

are usually tall and thin, with no compactness of form, while the facial expression in many instances bespeaks a "neurasthenia basis," and, according to Keith and Williams, in cases of visceral ptosis, there is commonly a marked forward curvature of the cervical region of the spine—"ewe-neck."

The examination of the abdomen should be made in both the upright and dorsal positions. In the former attitude one finds, in typical cases, the lower part of the abdomen flaccid and prominent, overhanging the symphysis pubis—the "Hängebauch" of the Germans (Fig. 5126), contrasting strongly with the upper quadrants which are usually flat or hollowed out. Meinert holds that such a pendulous abdomen holds a dilated stomach and not a dislocated one. It is in the dorsal position, however, that one gets positive evidence of the postural anomalies of enteroptosis. The epigastrium is usually flat and somewhat scaphoid, with widespread pulsations, while the peri-umbilical region is prominent. Peristaltic waves may be seen crossing the

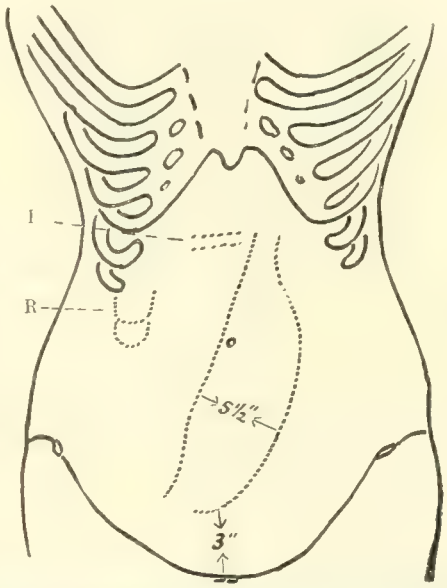

FIG. 5128.—Stomach Vertical or Nearly So. Located by illumination. The "corde colique transverse" is well shown. Right kidney (*R*) is prolapsed.

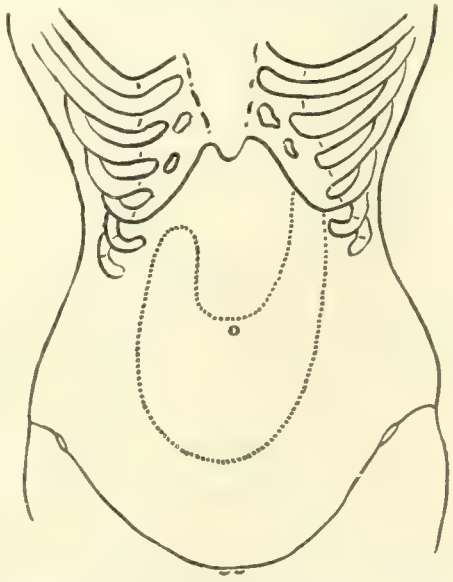

FIG. 5129.—Showing Tendency to V-shape of Stomach on Inflation.

abdomen from side to side; the recti abdominales are frequently widely separated, as may be shown either by palpation or by directing the patient to lift the head and

shoulders unaided by the hands or elbows, when a prominent central ridge appears running from the ensiform cartilage downward. The usual methods for determining the positions of the different organs should be resorted to: palpation and percussion for the solid organs, while inflation and illumination, as well as auscultatory percussion, may determine the situation of the stomach,

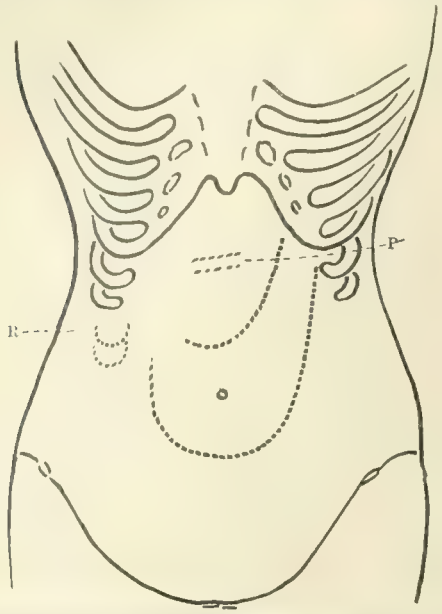

FIG. 5130.—Showing Gastroptosis and Nephroptosis. *P*, The "corde colique transverse." (Pancreas is well shown.)

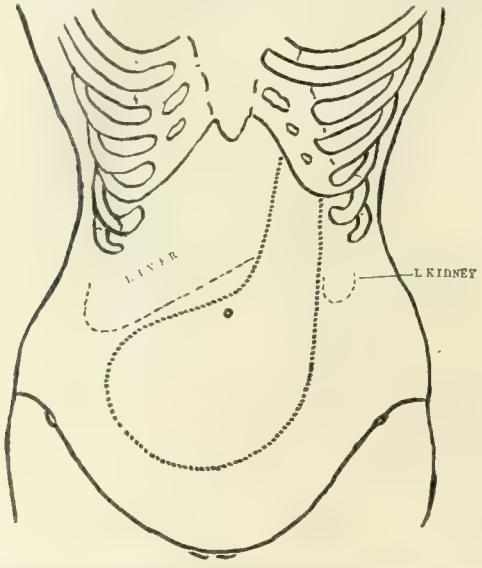

FIG. 5131. Showing Ptosis and Dilatation of Stomach. Ptosis of the liver and of the left kidney.

etc. Of these methods there seems but little doubt that inflation is the most accurate. It is important of course to distinguish between a displaced stomach and a dilated stomach. Indeed, when that organ is displaced it is usually dilated to some extent.

The organs usually found prolapsed, in cases of enteroptosis, are the stomach, the right kidney (movable or floating), and the colon (Fig. 5125). There is, however, increasing evidence to show that the liver is much more frequently dislocated than was at one time supposed. The left kidney and the spleen are implicated in this condition rarely as compared with the right kidney. The pancreas may be displaced also, chiefly at its head. Not infrequently the pelvic organs suffer the same displacement. The diaphragm and heart may participate in a general ptosis.

With reference to the determination of the position of the stomach, it is important to remember that normally the lesser curvature does not come into view when the organ is inflated, and that the whole of the organ lies above the umbilicus. Hence, when the lesser curvature is seen, and its normal relation to the greater curvature (four to four and one-half inches) is not greatly altered, gastroptosis is present, and in proportion as the lesser curvature approaches the umbilicus, or goes even below it, an increasing degree of gastric dislocation obtains. The stomach is sometimes seen in the oblique or almost vertical position (Figs. 5127 and 5128), and not infrequently the pyloric end is dilated, forming a three-quarter circle with the umbilicus as centre when outlined upon the abdomen. Again, the stomach may be somewhat V-shaped (Figs. 5129 and 5130).

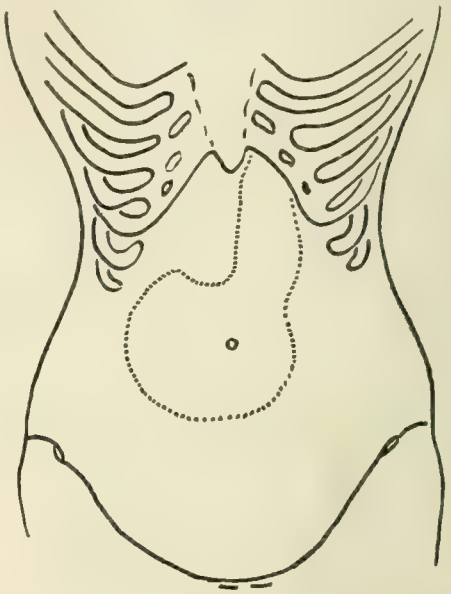

FIG. 5132.—From a Man with Kidney Freely Movable and Characteristic Symptoms.

What is the small band which is palpable running across the abdomen about two inches or so above the umbilicus? (Figs. 5128, *I* and 5130, *P*.) Glénard termed it "la corde colique transverse," and regarded it as the "colon transversum." There is good reason to doubt the correctness of this view. If the stomach is low the colon is generally lower, and in a case in which the band was most typically found by the writer, operation proved it to be the pancreas. In palpation of the abdomen Glénard laid special stress upon a test of considerable diagnostic value. The examiner, standing behind the patient, who is also in the erect position, places both hands flatly over the lower zone of the abdomen and applies firm and gentle pressure upward and backward. In the great majority of cases of enteroptosis this act affords considerable relief to the distressing dragging sensation felt in the epigastrium and abdomen. At the same time the result when "l'epreuve de sangle" is applied, is an index to the treatment. (I am greatly indebted to my house physician, Dr. J. R. Byers, for the accompanying illustrations.)

Stiller's Sign. (Costa fluctuans decima.)—Stiller re-

gards enteroptosis as of a neurasthenic origin, and looks upon the presence of a floating tenth rib as indicative of the presence of a neurasthenic tendency. Observations upon this point reported by Meinert, Zweig, Arneill, and others, go to show that this sign in the diagnosis of enteroptosis, or neurasthenia, is scarcely so important as Stiller would have it.

With respect to the relation of enteroptosis, more especially gastroptosis, to chlorosis, it must be said that it is not that of cause and effect—no characteristic blood condition is found in cases of enteroptosis, and many cases of chlorosis occur in which there is no evidence of visceral displacements.

Jaundice, which has been seen in several cases, may result from a variety of causes. "Gall stones are commonly, if not always present, in cases of enteroptosis." This statement, made by Dr. A. Keith, seems rather too broad, although it must be admitted "that the condition of visceral ptosis favors their formation." However, there can be no doubt that the altered relation of the bile ducts and organs, especially the right kidney, the liver, and the duodenum, might in a variety of ways cause obstruction to the outflow of bile and thus induce jaundice.

Pathology.—It may be well before taking up the diagnosis of this condition to consider more particularly the pathology of enteroptosis. The symptoms of enteroptosis may be accounted for by various theories, which for convenience fall under three headings:

1. The mechanical theory of Glénard.
2. The neuro-mechanical theory of Meinert.
3. The neuro-intoxication theory of Schwerdt.

The first theory, though not a purely mechanical one, does not ask for any antecedent nervous cause, but implies a weakness of the suspensory ligaments of the transverse colon, especially the colo-hepatic ligament. The descent, Glénard claims, begins at the hepatic flexure and the other events incident to the disease follow—entero-stenosis, due to a kinking of the colon at the point of prolapse, the gastroptosis, the constipation, auto-intoxication, the neurotic manifestations, etc.

Under the second theory Meinert attributes the symptoms associated with dropping of the viscera to the constant stimulation and irritation of the sympathetic nerves, as a result of pulling and stretching of these nerve fibres. The blood-forming organs and the general nervous system participate in this abnormal irritation and stimulation, and chlorosis, neuroses, and a variety of vaso-motor disturbances are thus induced.

Schwerdt believes that the nervous system is primarily at fault; the fibre of the individual is toneless, the functions of the abdominal muscles, both parietal and visceral, are not normal; intra-abdominal pressure is lessened, ptosis follows. There is a stasis in the blood and lymph vessels, the bowel contents stagnate and decompose, excretions accumulate; absorption of poisonous products goes on, and intoxication is the result—dyspepsia, headache, anæmia, palpitation, neurasthenia, etc.

Diagnosis.—In the great majority of cases one may suspect the condition from the complaints made by the patient—digestive disturbances, distress, not necessarily pain, in the stomach on getting up in the morning, or after being in the recumbent posture for some time, dragging under the right costal margin, a feeling as if something falls over to the left side when the patient turns on that side, constipation, lack of energy, and other neurasthenic symptoms. The patient is generally slender and of lean habit.

An examination of the abdomen, however, is necessary to correct or justify the suspicion derived from the complaints. The contour of the abdomen may further suggest a condition of splanchnoptosis and inflation of the stomach by means of tartaric acid and bicarbonate of soda, or air cautiously pumped in, readily and accurately serves to locate that organ. The solid organs may be palpated, and it is recommended to examine the liver while the patient is in the upright position. Displacements of this organ are doubtless much more frequent than might be supposed, judging from the results of examination in the dorsal position. The right lobe of the liver in some cases projects in a tongue-like process below the costal margin. It has been described as Riedel's lobe, and may occasionally be somewhat misleading. The test known as "l'epreuve de sangle," already described, should be applied in all suspected cases. It is scarcely possible, after a careful examination, to mistake enteroptosis for any other condition. Doubtless many

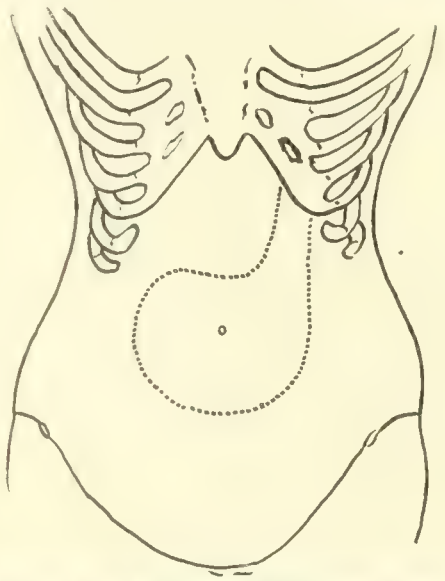

Fig. 133.—From a Case of Pulmonary Tuberculosis. Gastroptosis with dilatation of the pyloric end, showing as a three-quarter circle; the umbilicus as centre.

cases of gastric neurasthenia and of nervous dyspepsia would be cleared up by a careful search for visceral ptosis.

Among others at least two instances of mistaken diagnosis coming under the writer's notice may be recorded. In one, a diagnosis of malignant disease of the stomach led to a laparotomy revealing the pancreas as the palpable misleading mass, while in the other, recurrent jaundice was thought to be due to gall stones or a "sluggish liver," and the horseback riding, rowing, walking, canoeing, recommended for its relief, aggravated all the symptoms. On the other hand, there is danger of attempting to explain too many symptoms by visceral ptosis.

Prognosis.—Many patients recover entirely, losing all symptoms and signs of the disease. The majority may recover from the evil train of symptoms, the ptosis existing in part at least. It may be fatal as the result of the exhaustion and intoxication in extreme cases.

Treatment.—The indications for the treatment of enteroptosis as originally recommended by Glénard can scarcely be improved upon. They are as follows:

1. The intestines must be elevated and kept in their new position.
2. The abdominal pressure must be increased.
3. The bowels must be regulated.
4. The secretions of the intestinal glands must be increased.
5. The digestion and nutrition must be regulated and stimulated.
6. The whole organism must be strengthened.

If a cause can be fixed upon as inducing or aggravating the displacement, let it be removed. Those measures will best meet all these requirements which increase the strength and raise the tone of the whole musculature. It seems in most cases to be a question of nutrition, rest, good food, mild yet efficient purgatives, or better still enemata, occasionally gastric lavage, with drugs directed

against fermentative processes in the early stages of the treatment, as indicated. It is of the highest importance to increase the strength of the abdominal muscles by regulated exercise. Belts, or abdominal supporters, so highly recommended and in such variety, are of doubtful utility. Only those belts which increase the intra-abdominal pressure should be used. They encircle the abdomen and exercise the same degree of pressure over the whole abdominal surface. It is not only futile, but often harmful, to attempt to hold a kidney or a stomach in place by any special device externally applied.

With respect to surgical treatment of this condition, it must be said that it should be undertaken only after other methods have failed, and then only with the greatest care, especially in those cases in which the neurasthenic element is strongly manifest, for such patients are often worse rather than better after surgical interference. Duret first operated in 1894, lifting the stomach and fixing the serosa of the lesser curvature of the stomach to the parietal peritoneum and muscle of the anterior wall of the abdomen. Byron D. Davis (1897), Beyea (1898), Hartmann (1899), Treves, Bier, and Webster, have operated with varied success on similar cases. Beyea and Stengel shortened the gastric hepatic omentum and gastrophrenic ligament by plicating with multiple sutures, thus bringing the stomach up to its normal position. Webster, selecting those cases in which there was separation of the recti muscles, sought to increase intra-abdominal pressure by resecting the fascia of these muscles and then suturing the muscles together.

William Fawcett Hamilton.

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ERYTHROL TETRANITRATE, $C_4H_6(ONO_2)_4$, is obtained by the action of nitric acid on the tetratomic alcohol, erythrite, a substance found in several different lichens, especially *Rocella*. It occurs in colorless lamellæ, melts at 61° C. (142° F.), is insoluble in water, and dissolves readily in alcohol and ether. On percussion or when rapidly heated it explodes with great violence, and one fatality has occurred from its trituration with sugar of milk. In direct sunlight it turns yellow and gives off nitrous fumes.

The drug is a vaso-dilator, and its action differs from that of amyl nitrite and nitroglycerin in no essential except that it is slower in its onset and more lasting. It is said to take half an hour for the production of vaso-dilatation, and several hours for the effect to wear off. The dose is gr. ¼–i. (0.015–0.06 gm.), most conveniently administered in tablet triturates. Bradbury recommends 3 i. (4 c.c.) of a 1 in 60 alcoholic solution repeated every four to six hours. *W. A. Bastedo.*

ERYTHROMELALGIA.—This affection was originally described by Weir Mitchell in 1872 as follows: "A chronic disease, in which a part or parts—usually one or more extremities—suffer from pain, flushing, and local fever, made far worse if the part hangs down," and writers since then have not been able to agree upon a definition more satisfactory than this descriptive one. Up to the present time about one hundred cases have been reported and discussed by neurologists and pathologists, the questions of its pathogenesis, and of whether the affection is properly a distinct disease or entitled only to be called a group of symptoms, having excited much interest. To these topics we shall return in their proper place.

The subjects of erythromelalgia are usually middle-aged people, sometimes young adults, but seldom children. Many more males are attacked than females, and the predisposing causes are such as men are more liable to than women, viz.: occasionally traumatism, as from a stone falling upon the foot, exposure to wet and cold, especially when repeated, long standing at fatiguing work, sometimes exceptionally exposure to heat, as in working at a furnace. Also malaria, syphilis, anæmia, alcoholism, hysteria, and dyspeptic states are all believed to stand in a causative relation to it. It is also found associated with various other general diseases, and particularly those of the nervous system. Reynolds mentions one case as coming on suddenly soon after confinement.

Symptoms.—The most distinctive and fundamental symptoms are those originally emphasized by Weir Mitchell. He also in his most recent paper on the subject reminds us that the pure type of symptoms should be looked for in the youngest class of patients, for in those who are more advanced in life diseased conditions of the arterial or nervous system may exist independently of erythromelalgia and lead to confusion. The local symptoms involve almost exclusively the peripheral parts of the extremities. The three characteristic symptoms are localized *pain*, *redness*, and *swelling*, suggestive of inflammation and yet to be carefully discriminated from it. The *pain* is apt to be the first abnormality to attract attention, involving most frequently the great toe, the heel, the ball of the foot on its inner or outer side, or the metacarpo-phalangeal articulation, less frequently the upper extremities, or exceptionally other parts. These pains are described as burning, irritating, piercing, and as sometimes of intolerable severity, "as if the part were being destroyed by fire" (Kahane). They are at first occasional, coming on at varying intervals or after special exciting causes; then they become intermittent and then constant, although there are reports of cases in which they finally ceased. The latter part of the day, especially after exhausting labor, hot weather, a hanging position, also motion, all intensify the suffering; while on the other hand cold, either of the weather or of applications, rest, and an elevated position of the affected part give relief. Thus it is quite characteristic for patients when the hands are the seat of the local trouble to carry them crossed upon the chest or raised above the head (Barlow).

The redness, which is the second prominent local manifestation, accompanies the pain, and its tint is variously described as fire-red, violet, livid, the latter verging sometimes into a cyanosis. Weir Mitchell calls it rosy red and congestive, and the disease itself has been called *red neuralgia*.

The swelling comes on gradually, is localized like the pain and redness, especially about the joints, but is not marked by pitting. It is increased by motion. Nor is it strange that this association of symptoms has in some cases led to a diagnosis of deep-seated inflammation, for

the relief of which incisions have been made, which, however, revealed nothing.

The seizures thus characterized were called by Mitchell "vascular storms." They may last for several hours or may extend to days or weeks, the local feature sometimes extending to parts not originally involved. The seats of attack are sometimes symmetrical, sometimes not. But in addition to the symptoms already mentioned others show themselves, which have been considered not characteristic of erythromelalgia, and which are not constant, but still may be of importance as bearing upon its pathogenesis. Thus Elsner and Barlow speak of hyperidrosis accompanying the paroxysm, of "innumerable droplets of perspiration standing upon the skin at the time of the most acute pain." There may be a condition described as local asphyxia, which may merge into cyanosis. The pulse is often quickened, which, taken in connection with the changes in the circulation, may be an index of more than local vaso-motor disturbances. Lesions of sensibility are frequently present, hyperæsthesia and paræsthesia most commonly, but are by no means constant enough to be regarded as characteristic of the disease; nor is the motor function often interfered with, the lesions when occasionally encountered in the more advanced cases being present as weakness and paresis. There is sometimes muscular atrophy. Reflex irritability is infrequent. The *trophic* lesions associated with the local manifestations are frequent and multiform. The skin may be either thickened or show changes analogous to the "diffuse idiopathic atrophy of the skin," of dermatologists, as in a case reported by Schütz. There are sometimes pigmentation and œdema, and lumpy alterations of the joints and nails; also rhagades and ulcers may develop. It is also quite common to find nodules or papules on the reddened and painful areas (Kahane). One other symptom which sometimes presents itself is gangrene, considered by some to be a feature of indubitable cases of erythromelalgia, its occurrence depending upon the greater or less severity of the disease (Sachs), and by others as indicating its alliance with Raynaud's disease.

Such, then, are the local changes, which, says Reynolds, are the only symptoms in twenty per cent. of the cases. The disease is essentially chronic and of very gradual development. Barlow refers to one case which lasted for twenty-seven years, the affection limited to the sole of one foot; Elsner to one involving the left index finger only, for sixteen years, amputation of the finger finally relieving all the symptoms.

Interesting as erythromelalgia has proved to neurologists, it is its pathological position which has given rise to the most discussion, for its symptomatology is well recognized and its diagnosis not ordinarily attended with difficulty. Still there have been but few autopsies reported. The opportunity of examining amputated parts has indeed been availed of, but the findings have not led to general agreement as to its pathological anatomy, and Cassirer, writing in 1901, says: "We are still to-day far removed from any certain knowledge of the pathological anatomy of erythromelalgia." Consequently its pathogenesis has not been satisfactorily determined. Nor have the questions whether it is ever an idiopathic disease, or whether it is merely a "symptom complex," associated with various other diseases, been answered conclusively. It would be impossible here to go into the details of this inquiry, and it has seemed best to give as nearly as possible in chronological order the views of the principal authorities, which will at all events show the trend of professional opinion and develop the mooted points.

Weir Mitchell in his earlier publications refrained from any positive expression of opinion as to the origin of the malady, but later (1878) regarded it as "a *vaso-motor neurosis*, which might occur either independently or in association with spinal or cerebral disease, where some distinct lesions of definite regions might ultimately be discovered." Subsequently he expressed the view that in erythromelalgia a neuritis of the finest nerve twigs may be present. Lewin and Benda, writing in 1894, most thoroughly discussed all the cases that had been reported up to that time. They classify these cases under three headings: 1st. Erythromelalgia in organic diseases of the central nervous system. 2d. In functional diseases of the central nervous system (neuroses). 3d. As a peripheral affection (neuritis and neuralgia), the latter group embracing half of all the cases. The vaso-motor symptoms are always secondary to the neuralgic pains. In answer to the question whether it is an independent disease, their conclusion is that it is not a disease *sui generis*, but may be associated with various peripheral and central diseases of the nervous system.

In 1895 Eulenburg wrote that he had reasons for "thinking that the starting point of the disease may be found in certain sections of the gray axis of the cord, especially in the posterior and lateral gray substance, and the associated fasciculi," an opinion which has had great weight.

Auerbach in 1897 published a report of the first complete autopsy made on a case of this disease. There was a normal condition of the peripheral nerves and spinal ganglion cells, marked degeneration of numerous radical fasciculi (Wurzelbündel) in the cauda equina, on one side more than the other, belonging to the first or second sacral nerve and the last lumbar nerve. Pronounced ascending degeneration in the cord."

In 1899 Weir Mitchell and Spiller report that in examining an amputated toe from a patient with erythromelalgia there were found a high degree of degeneration of the nerves, which were almost completely converted into connective tissue, also extreme changes in the vessels, thickening of the media, hypertrophy of the intima, and in places complete closure of the lumen of the artery; and on this finding peripheral neuritis was assumed as the basis of the disease. In this article the opinion is still held that certain cases may be due to some form of spinal disease, but the idea of a nerve-end neuritis is urged. These examinations and others give greater definiteness to the discussion of the pathological relations of the central and peripheral organs in the development of the disease. In Dehio's case 4 cm. of the ulnar nerve and an equal length of the ulnar artery were removed just above the wrist for erythromelalgia involving the hand. The little finger improved, but the rest of the hand remained unchanged. Examined under the microscope the piece of the nerve was found normal, but the artery showed marked arteritis of the middle and inner coats and some diminution of the lumen. Barlow indicates three directions in which inquiry as to the pathology should extend: 1st, to the peripheral nerves; 2d, to the brain and cord, especially in regard to the vaso-motor centres; and 3d, to the blood-vessels. He declares that the disease has been generally regarded as a vaso-motor neurosis or paralysis, and concludes that "in the absence of obvious nerve disease to explain the arterio-sclerosis we are led back to the hypothesis that the chief fault lies with the vaso-motor centres and their abnormal efferent vaso-motor impulses leading to dilatation of the vessels and consecutive disease induced thereby. Some peripheral strain or irritation may have been transmitted to the vaso-motor centre as the original cause of the disturbance." He further expresses the belief that probably the change in the vaso-motors starts centrally, especially in the generalized cases of the disease, although it is more reasonable to suppose that in uncomplicated cases the primary change starts at the periphery. The question whether erythromelalgia is an idiopathic affection or should be considered merely a group of symptoms appearing in association with various primary diseases has brought out a diversity of opinion. Collier in 1898 says it is not now regarded so much as an idiopathic disease as a group of symptoms occurring in other affections, and Kahane, writing in 1900, quotes Lewin and Benda, Eulenburg and Levi as holding the same view, and says the conclusion reached in all the larger comprehensive statements about erythromelalgia is that it is no individual disease, but a symptom-complex accompanying various other diseases of the nervous system.

Kahane himself, however, finally gives as his own opinion that it should be ranked among the acropathies, which he defines as those affections which are localized in the peripheral parts of the limbs and as the ultimate basis of which are assumed lesions of a vaso-motor nature. There is great difficulty in determining whether the nerves or the vessels form the starting point, whether we have to do with an irritation of the vaso-dilators or a paralysis of the vaso-constrictors. He says, in conclusion of a long and careful consideration of the question, that there are two points that one can be sure of: 1st, that erythromelalgia belongs clinically to the group of acropathies; 2d, that it is to be referred to a disturbance in the relation between the systems of the nerves and blood-vessels quite without regard to the question whether it is of functional or anatomical, central or peripheral nature. In his conception it is a phase of disease that occurs in one series of cases independently and in another as an attendant phenomenon of other diseases.

Sachs had found the blood-vessels diseased in most cases, but the nerves not in many; the changes in the latter he believed to be secondary. He says erythromelalgia occurs as an independent group of symptoms, even if not an individual disease. In uncomplicated cases it is probably to be referred to disease of the peripheral arteries. The obliterating arteritis may be indirectly connected with central disease, but may be wholly independent of such influences. In 1901, Elsner, on examination of the arteries in cases that he saw, found them the seat of occasional slight thickening of the intima, but the nerves normal. He calls attention to several cases in which gangrene of the extremities occurred. He believes that erythromelalgia cannot at present be defined as a disease *per se*. Cassirer, on the contrary, is constrained to place himself among those who believe the disease to have a certain idiopathic character, while recognizing like others one class of cases of a peripheral and a second of a central origin. Allchin and Saville regard the disease as of vaso-motor origin, probably allied to Raynaud's disease, the former speaking of it as an expression of vaso-motor ataxia. Shaw in 1903 analyzes nine cases and reports the results of the examination of amputated toes in three cases, stating that "vascular change was present in all, mostly an increase in the intima of the arteries and occasionally thrombosis and changes in the inner coat of the veins. The nerves were investigated even to their terminations, and no degeneration was found, nor was there any suggestion of increase of fibrous tissue in the trunk of the nerves." (Compare Mitchell.) He says: "In no case has recent degeneration of nerve fibres been demonstrated, and in not one of the nine cases analyzed was anæsthesia ever present." He concludes that erythromelalgia when occurring independently of central nervous change is associated with but one morbid picture, that of local vascular change. Taubert finds erythromelalgia traceable to disease in the lateral and posterior columns of the cervical cord (see Eulenburg and others). Reynolds calls the disease a vaso-motor neurosis, and argues in favor of the theory of primary vaso-motor dilatation of the arteries followed in the way of compensation for this vaso-motor paralysis by thickening of the coats of the arteries so as to narrow the lumen and stream of blood (quoting Delafield, Thoma, and Barlow in support of his views). Starr, sketching the phenomena of the "vascular storm," says: "The dilatation of the arteries in the extremities results in an extreme condition of redness and sensation of heat and pain. After hours of this the extremities may suddenly become cold, pale, or blue and shrivelled up, presenting the appearance of the hands after long soaking in hot water; and this alternation of distention and contraction of the blood-vessels constitutes the symptomatology of the disease. It appears to be a pure vaso-motor neurosis, but it is rarely if ever attended by any trophic disturbances of the skin or nails, such as occur in neuritis, and no pathological observations are at hand to establish the hypothesis that there is a true neuritis of the vaso-motor nerves."

If, thereore, we should venture upon a rough summing up of the principal pathological features of erythromelalgia as indicated in the preceding brief synopsis of recent authorities we should say that opinion was settling upon the following beliefs: (1) The disease is considered a vaso-motor neurosis (angioneurosis, Oppenheim); (2) the attribution of the group of symptoms to disease of the posterior and lateral spinal gray matter, when it would be called secondary, and to as yet undetermined causes of peripheral origin, where some would call it clinically idiopathic or *sui generis;* (3) its association with the acropathies and sometimes with Raynaud's disease; (4) there is much more evidence connecting the disease locally with alterations of the blood-vessels than of the nerves, but good authorities deny that we are yet in position to pass finally upon its pathology.

The TREATMENT of erythromelalgia can hardly be said to aim with hopefulness at more than the alleviation of some of its most distressing symptoms, proof of which is found in the long list of the various means employed. Weir Mitchell's recommendation of rest, cold, and elevation of the limb affected has been found of value, based as it is upon well-known observations of patients that the opposites of these increase their sufferings. Other measures to be noted are hydrotherapy, electricity (Eulenburg and Schütz found benefit from the use of the constant current), massage (although Barlow says it is of doubtful value and unbearable during the paroxysms). Of course antisyphilitic remedies are indicated in cases in which that disease is believed to underlie or complicate erythromelalgia, and among drugs which are more or less approved are arsenic, antipyrin, the bromide of potassium, morphine (Morgan reporting a case of recovery after hypodermic injections of morphine and atropine twice a day for three weeks), the salicylates, atropine, and ergot internally as well as ichthyol externally. It should also be remembered that spontaneous recovery has taken place in some cases. Further than this, the several cases referred to above are evidence that surgical measures, such as the stretching of nerves, their resection, and the amputation of toes and fingers, have brought relief in certain instances. It should be noted, however, that gangrene followed operative procedures upon nerve and vein in one case of Weir Mitchell's and upon amputation of a toe in another.

The references given below are mainly to the chief articles of the last three years, the reader being referred to the essays of Lewin and Benda and of Kahane for full bibliographies. *J. Haven Emerson.*

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EUCAINE is a name applied to two different but closely allied local anæsthetics distinguished as *Alpha-eucaine* or *Eucaine "A"* and *Beta-eucaine* or *Eucaine "B."*

The anæsthetic effect of cocaine, which is methyl-benzoyl-ecgonine, $C_{17}H_{21}NO_4$, was found to depend on the presence of both the methyl and the benzoyl groups and not on the ecgonine radical. So with the desire of obtaining the anæsthetic effect of cocaine without its toxicity, other methyl-benzoyl compounds were designed. Of these Eucaine "A" was submitted to the profession, and was for a time extensively employed; but its very irritating effects have so militated against its desirability that it has been largely replaced by its congener, Eucaine "B," a compound of less toxicity and less irritating properties.

Alpha-eucaine, $CH_3.N.C_2.(CH_3)_2.(CH_3)_2.(CH_2)_2.CC_6H_6COO.COOCH_3$, is methyl-benzoyl-tetra-methyl-hydroxy-piperidine-carbonic-acid-methyl-ester, a derivative of tri-acetone-amine. Its hydrochloride occurs as a bitter white crystalline powder soluble in 10 parts of cold water, 7 of boiling water, less than 2 of alcohol, and 13 of glycerin, and is very slightly soluble in ether and the fixed oils.

Beta-eucaine, $H.N.C_2.HCH_3.(CH_3)_2.(CH_2)_2.C.C_6H_5COO.H$, benzoyl-vinyl-diacetone-alkamine, is also a bitter white crystalline powder, and its hydrochloride dissolves in 23 parts of water, 12 of boiling water, 30 of alcohol, and 35 of glycerin. It is insoluble in ether and almost insoluble in the fixed oils.

Both eucaines have the nature of alkaloids, and their hydrochlorides have been the salts in common use; but the acetate of beta-eucaine is now recommended as it is readily soluble in water. The solutions of eucaine salts are not decomposed by boiling, so may be sterilized.

The pharmacological action of the eucaines has been studied by Cushny, Vinci, Ver Eecke, and others. The salts are not absorbed by the unbroken skin, but, applied to mucous membranes or injected into the tissues, they paralyze the sensory nerves and their terminal endings at the site of application and are powerful local anæsthetics. They are said to produce local congestion in mucous membranes.

In large dose they weaken the heart by direct depression of the cardiac muscle and its contained ganglia, and in addition lower blood pressure by dilatation of the arterioles. The respiratory centre is at first stimulated, later paralyzed, so that death takes place from asphyxia (paralysis of respiration). The cerebral centres are stimulated with the production of tonic and clonic convulsions; later they are paralyzed. There is no dilatation of the pupil or disturbance of the accommodation of the eye, but the conjunctiva is congested. The superficial epithelium of the cornea is not affected. The kidney cells are stimulated and the quantity of urine is increased, with increased elimination of nitrogen, phosphorus, and chlorides. The drug is not found in the urine, and apparently undergoes decomposition in the body.

To produce general poisoning in rabbits and guinea-pigs it requires 0.15–0.2 gm. of eucaine "A" per kilo, and 0.4–0.5 gm. of eucaine "B." Cocaine is four times as poisonous as eucaine "B," and only slightly more toxic than eucaine "A."

The uses of beta-eucaine as a local anæsthetic are practically those of cocaine, so we need not here enumerate its therapeutic applications. The consensus of opinion among surgeons (Bier, Bainbridge, Moyer) would seem to indicate that it is weaker as an anæsthetic than cocaine, whether employed subcutaneously or in spinal analgesia. Wallis found that the amount required for a small operation averaged ʒ i.–iss. (4–6 c.c.) of a four-per-cent. solution, but G. W. Crile performed a painless duodenostomy with 8 c.c. (ʒ ij.) of a two-per-cent. solution.

Nearly all writers agree that eucaine tends to increase a hyperæmia of the conjunctiva or nasal mucous membrane, and Dawbarn and others prefer it for the removal of tonsils, adenoids, and other hypertrophied tissues, as it does not cause a shrinkage like cocaine. Poole prefers cocaine in iritis, as eucaine increases, or at least does not decrease, the anterior congestion.

In our experience eucaine applied to mucous membranes is slower in its action and much weaker than cocaine; used subcutaneously it is somewhat weaker. We had several cases of local gangrene following its hypodermic use in abdominal and pleural tapping, though in each of these instances the injection had been preceded by the ethyl-chloride spray. Cocaine under similar conditions never produced a slough. Da Costa noted a slow, persistent sloughing, especially in fatty tissue, bursæ, or tendon sheaths. He also noticed inflammation following its use in the bladder. Shastid reports the occurrence of amblyopia, rapid pulse, and delirium following the application of a five-per-cent. solution to the inferior turbinate.

Beta-eucaine is, then, a drug of anæsthetic action resembling that of cocaine, but somewhat weaker. It produces hyperæmia rather than the ischæmia of cocaine, and has no effect on the pupil, accommodation, or the corneal epithelium. In the ordinary dosage it is nontoxic, and is reported to be well borne where there is an idiosyncrasy against cocaine. Lilienthal has frequently used four to ten grains without unpleasant consequences. No eucaine habit is known. The drug keeps indefinitely and can be sterilized by boiling.

Solutions of one- to four-per-cent. strength in normal salt are commonly employed, but stronger solutions, obtained by heating the liquid and using warm, are sometimes preferred. Von Mikulicz uses the following: ℞ Cocainæ hydrochloridi, 0.5 gm. (gr. viiss.); beta-eucainæ hydrochloridi, 0.5 gm. (gr. viiss.); sodii chloridi, 2 gm. (gr. xxx.); aquæ, q.s. ad 1,000 c.c. (ʒ xxxii.).

W. A. Bastedo.

EXOPHTHALMIC GOITRE.—(Synonyms: Graves' disease; Basedow's disease.) These names have been indifferently used during the last sixty or more years to express a fairly well-defined disease in which more or less enlargement of the thyroid, protrusion of the eyes, and certain nervous disturbances (including tachycardia) form the prominent symptoms. The Irish physician, Graves, who described the coexistence of palpitation of the heart with enlargement of the thyroid as an affection more or less related to hysteria, was antedated in his observations by Parry, who mentioned the same combination together with exophthalmos in 1825. Some years later Basedow also observed the existence of exophthalmos in similar cases, and gave the description which has connected his name with the disease. Charcot, too, in 1844 and 1845 described such cases at the Salpêtrière. Since their time an enormous literature has appeared in which, while the objective descriptions remain very constant, the most divergent theories have been advanced to account for the symptoms. These we may detail in discussing the etiology of the disease.

Exophthalmic goitre is an affection which occurs most frequently in women, although cases are by no means rare in which the same phenomena are seen in men. No very precise age limits can be set, but the majority of the cases appear to begin after the age of puberty, and to increase in number as the climacterium is approached, the onset being most frequent, according to Osler, between the ages of twenty and thirty. No particular station in life seems to predispose to the disease, but it is usually observed that the individuals belong to neuropathic families in which cases of epilepsy, hysteria, chorea, or even some form of insanity have occurred. Combinations of epilepsy and exophthalmic goitre in the same person have been described,[1] in which cases the epileptic seizures usually give place to the symptoms of the other disease. Exophthalmic goitre is a very widespread disease, not at all localized in certain areas, as is the case with other forms of goitre and with endemic myxœdema or cretinism. Indeed, although cases in which exophthalmic

symptoms supervene after the long existence of the ordinary type of goitre are not unknown, the disease seems to be no more frequent in those regions where goitre is endemic than elsewhere, and the coincidence of the two conditions must be considered accidental. Instances of the coexistence of exophthalmic goitre with myxœdema have also been observed,[2] which, although probably accidental and not indicating any close relationship between the two conditions, have a significance which will appear later.

Symptoms.—The onset is sometimes very slow and gradual, in other cases it is extremely sudden, and the symptoms reach their maximum of intensity in a very short time. Usually, but not always, such an onset is ascribed to sudden violent emotional disturbances, such as a fright or great sorrow, etc., after which the patient feels demoralized and incapable of effort, and the palpitation of the heart and tremors begin. Prominence of the eyeballs may be the first thing observed, and is noticed by the friends before the patient herself appreciates it.

Of all the symptoms perhaps the most constant are those referable to the heart and circulatory system in general, and these may be considered under several heads. First of all and most noticeable is the violence of the heart's action—a pounding heart beat that may sometimes be violent enough to keep the patient awake can be felt over a wide area. Loud systolic bruits can often be heard over the apex and base of the heart and along the vessels. The pulsation of the arteries is extraordinarily violent in many cases and is readily visible in the extremities. There is usually a widespread dilatation of the capillaries also, and sometimes a venous pulsation can be made out. The dilatation and violent pulsation of the vessels are especially noticeable over the enlarged thyroid and in the eye grounds.

Then next in prominence is the tachycardia, which may reach the highest degree. Usually this develops gradually and the pulse rate increases from normal up to 130 to 150 or more in the minute. In a case recently observed in the Johns Hopkins Hospital, a rate of 200 per minute was maintained for days. The tension in such cases usually remains high, and the volume full. F. Müller[3] gives a sphygmographic tracing in a case whose pulse rate at the time was 176, in which this is illustrated, there being a sharp initial elevation with frequent bigeminal pulsation. Recent researches seem to show (Donath,[4] Spiethoff[5]) that the blood pressure is in some cases increased, in some diminished, but by no means always increased.

Variations in the pulse rate are very marked, and excitement or exertion has a much greater influence than in a normal individual. In some instances it is impossible to escape from the idea that exhaustion of the heart muscle must play a part in the final dissolution of the patient.

Referable to the central nervous system more directly we find a variety of symptoms, of which perhaps the most prominent is the tremor. This is involuntary and fine for the most part, leading to a fine trembling of the hands, muscles of the face, and indeed of any and all of the muscles indifferently. It is most noticeable to the patient in the attempt to perform fine co-ordinated movements. Writing becomes difficult or impossible, and the characters show a tremulous irregularity. Fibrillary twitchings of the tongue are usually present, and may be so extensive as to produce a wave-like undulation over the surface of that organ. Definite spasms and twitchings of various muscles may occur too, even producing in some cases the condition of tetany, such as has been described in thyroidectomized animals. Epileptiform seizures are not unknown, and may suggest an extreme manifestation of the tetanic condition. The explanation of these phenomena will be further discussed in treating of the etiology.

The other symptoms referable to the nervous system are chiefly psychical. Early in the disease the patients feel themselves to be irritable and excitable. The friends observe a change of disposition, very different from that observed in the development of myxœdema. Instead of becoming sluggish and apathetic, with all the mental faculties dulled, these patients are keenly susceptible to every outward stimulus, and the mental reaction is a relatively intense one. In some respects this receptive and reactive state may resemble in a mild way that seen in the maniacal stage of the maniacal-depressive insanity. A feeling of anxiety often dominates the mental state and the excited patient becomes a prey to groundless fears. Insomnia may be persistent, much to the exhaustion of the patient. In other cases fantastic dreams occur with great frequency, and may pass over into the waking state, so that the patient has but to shut her eyes to see all sorts of forms move about her, or even in broad daylight the hallucinations may occur. Delirium and the wildest maniacal excitement, or stupor and even unconsciousness may come on late in the disease.

The exophthalmos is not an invariable feature, although it is very frequently present (Fig. 5134, *A* and *B*); it may be unilateral, but is usually bilateral. In its onset it becomes, as a rule, gradually more and more noticeable, but sometimes, as it is alleged, after a sudden emotional shock it may appear and reach a high grade within a very short time. The actual extent of the protrusion of the eyeball it is difficult to measure, although methods have recently been devised which will render such measurements more exact. It is most noticeable in the widening of the aperture of the lids which it produces, and by the staring expression which it gives to the face; but it must not be forgotten that the individual variations in normal people in this respect are very great. In extreme cases, however, such as one of Basedow's, the eye may be actually dislocated from the orbit. Many consequences of this protrusion have been noted in the literature, and as signs of the exophthalmos they bear the name of their observers. Graefe, for example, noticed that in lowering the eyes the upper lid did not follow and keep the sclera covered as in the normal eye—the so-called Graefe's sign. Stelwag's sign consists in the widening of the palpebral aperture; Möbius' sign, in the lack of normal convergence of the eyes.

Pupillary changes are rarely if ever seen, and no definite retinal alterations have been found, nor is there any disturbance of sight from the exophthalmos proper. Winking is much less frequently carried out, however, than in the normal eye, and in cases in which the eye projects far from its socket the eyelids never quite cover the eyeball. The consequence may be that the proper moistening of the surface is interfered with, and a band-like area across each eye, passing over the cornea, becomes dried and opaque. Ulceration and infection of this dried area, which becomes wider with the increased protrusion, leads to complete opacity of the cornea and loss of vision in that eye. The infection may even go on to involve the whole eye and result in its entire destruction.

The absence of pupillary disturbances is particularly significant in connection with one of the theories as to the etiology of the disease, as will appear later.

No special disturbance of the urinary secretion seems to occur with this disease, although glycosuria has been observed in some cases and polyuria in others.

Digestive disorder and disturbances of the general metabolism, however, are almost constant, and have an extremely important bearing upon the prognosis.

Loss of appetite is very common, and the patients waste away perhaps as a result of this. On the other hand, a ravenous, insatiable appetite is sometimes observed, but strangely enough with the same progressive emaciation. F. Müller[6] describes most graphically this curious phenomenon. "The food prepared for this patient, quite enough for the nourishment of a robust person, was not enough for her, and she gathered up every scrap of food that was left by the other patients in the ward. One found her almost always eating, and it was curious to see her, as with wide open, eager eyes she stared into her plate and ceaselessly chewed and swallowed."

There are, however, variations in this emaciation, such

that while at times the patient loses rapidly in weight, there come periods during which she recovers almost all that was lost, and Huchard speaks accordingly of "crises d'amaigrissement." The loss of weight may be enormous and astoundingly rapid. One of Müller's patients lost fifty pounds in nine months, reaching then a weight of fifty-four pounds. Curiously enough the emaciation may not be general but limited to one portion of the body, either to one side or to the upper part, while the lower extremities remain unaltered. von Schrotter[7] describes such a case in which the very fat legs contrasted sharply with the wasted chest and shoulders.

Diarrhœa, of a most persistent character, is often observed, and may aid greatly in producing the emaciation. It seems possible that it may be due to an increased activity of peristalsis dependent upon some such nervous influence as produces the general tremor. Incidentally, too, it may be remarked that it seems possible that in those cases of persistent diarrhœa which are associated with tetany there may be an underlying cause for both, similar to that at work in the production of the disease under discussion.

Symptoms from the genital apparatus are very inconstant and difficult to explain. There is sometimes a cessation of the menses, and there have been instances in which pregnancy has had a favorable influence upon the course of the disease.

Changes in the skin are frequent and of many sorts. Very characteristic is the profuse and continued sweating, which is no doubt due to the central irritation of the secretory nerves. It is frequently such as to bathe the patient constantly and to keep the skin in a sodden condition, from which results the increased electrical conductivity noted by Charcot and others. Annoying sensations of heat, accompanied by flushing of the skin, frequently occur, while the general temperature is normal. Other changes, difficult to explain, also appear, such for example as the extensive pigmentation of the skin, which may be almost like that observed in Addison's disease. An instance of this is the above-mentioned case of von Schrotter. So, too, urticaria, erythema, localized œdema, scleroderma, loss of hair, swelling of joints, atrophy and hypertrophy of breasts, etc., occur, and are usually explained as dependent upon disturbances of the trophic nerves.

A. B.

FIG. 5134.—Case of Exophthalmic Goitre showing Exophthalmos and Goitre. *A*, Front view; *B*, side view.

Dyspnœa and labored breathing may come on, especially after exertion, and occasionally there is a dry cough which is very wearing, but which seems not to depend upon any actual pulmonary lesion.

Finally the thyroid shows fairly constant changes, which are recognizable clinically (Fig. 5134, *A* and *B*). The enlargement is usually diffuse and bilateral, but may not be extreme. Frequently it is so slight as to be hardly noticeable.

In all cases, however, the thyroid is somewhat increased in consistence and may sometimes become very hard. The vessels which course over it are generally widely dilated and pulsate violently, and to this great vascularity and hyperæmia is due in large part the enlargement of the gland.

PATHOLOGY.—Numerous autopsies have been performed on these cases, and the most painstaking examination of the viscera made without as yet any constant lesion having been discovered which can be considered explanatory of all these symptoms. Especial attention has been directed to the nervous system and to the thyroid, and the description of the changes in these can therefore be made more minute.

In the central nervous system no definite constant changes have been discerned in the cerebral cortex nor in the lower portion of the brain or cord. Only Mendel[8] and his students have found atrophy of the corpus restiforme on one side with a similar atrophy of the solitary bundle on the other side, and this he brings into causal connection with the disease. It is, however, far from constant, and it is hard to explain a general condition by a one-sided lesion.

The sympathetic ganglia in the neck have also been

examined with great care, but Ehrich,[9] who from his cases was able to find degenerative changes, thinks them entirely secondary. Others find no alterations whatever in these ganglia and nerves.

Müller found degenerative changes in the trunk of the vagus nerve, but decided that these were secondary.

The alterations in the heart are by no means constant nor characteristic. Dilatation is sometimes found at autopsy, hypertrophy occasionally, while degenerative changes are frequent.

It is in the thyroid that the most characteristic and constant changes are met with. The gland is usually but not always enlarged, and its consistence much increased. No adequate idea of the vascularity is gained from the inspection of the specimen after death, but at operation it is found to be extraordinarily rich in widely distended vessels, which pulsate violently, and which from the friability of their walls (Kocher,[10] Ehrich[11]) render the operation for the extirpation of the gland a difficult one. The surface is often somewhat nodular and the capsule thickened. Section of the gland shows that it has not the translucency and brownish-red color of the normal gland, nor its gelatinous elastic consistence. Instead it is hard and resistant, and of an opaque pinkish-gray color, the cut surface having a rather lobular, roughened appearance. (Figs. 5135 and 5136.)

Microscopically there is usually made out a great increase in the connective tissue throughout the gland. Strands of fibrous tissue run through it from the capsule and produce a sort of indefinite lobulation. More striking, however, is the alteration in the alveoli. Instead of preserving a more or less uniform roundness, they are distorted into the most complicated forms, and their

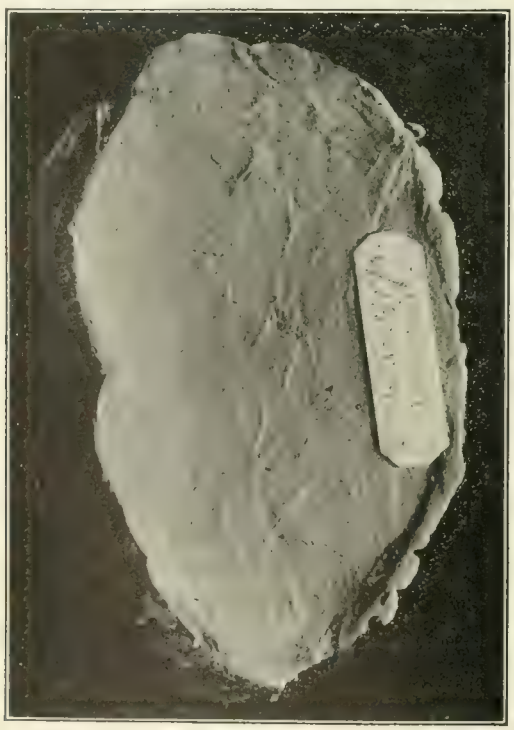

FIG. 5135. Exophthalmic Goitre. Thyroid lobe in section from case illustrated in Fig. 5134.

walls plicated and corrugated until the outline is an extremely irregular one. By many authors papillary outgrowths from the walls have been described, but Ehrich claims that these appearances are merely due to the irregular line of section of folds in the wall.

The cells are irregular in height and outline, and are often vacuolated and ragged, and contain more abundant fat globules than normal. There is much variation in the size of the alveoli, the distended irregular ones being frequently long drawn out and sometimes even com

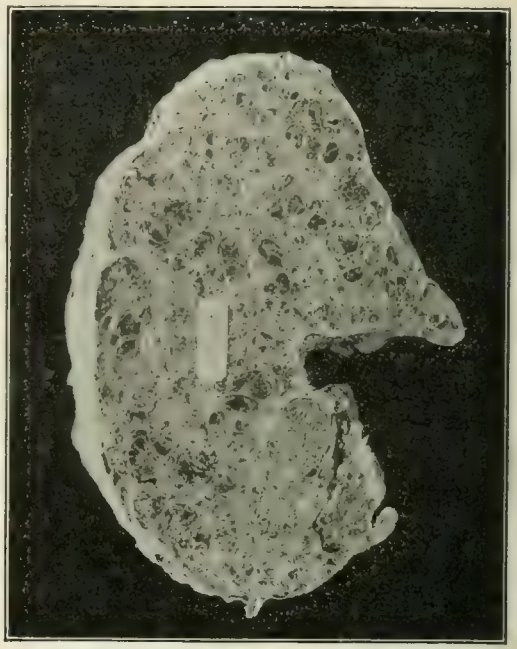

FIG. 5136.—Adenoma of Thyroid, or Colloid Goitre.

municating with one another, while others are small and so packed with cells that there is no real lumen. Mitotic figures are rare. Indeed Ehrich states that proliferation occurs only by amitotic division, and is not a prominent feature, but that the enlargement of the gland is largely due to the distention of the alveoli. The general trend of opinion, however, is toward the idea that there is a hypertrophy by cell proliferation.

We may pass over the histological details of the process of secretion as observed in these cases by Farner, Ehrich, Haemig, and others. Suffice it to say that while in some cases the process of secretion seems active enough, and the alveoli are filled with a stainable colloid material, in the majority the secretion of this stainable colloid is not evident, the cells have become high and vaculated, and whatever secretion there is, is of the non-staining or chromophobe type of Andersson. The alveoli in these cases are empty of colloid, and contain only the débris of cells and fine ragged strands of granular material.

As to the removal of the colloid material from the gland there is still some doubt. Many authors have described the presence of a material staining like colloid in the lymphatics and interstitial spaces, while others have even declared its presence in the veins and arteries. Thus Farner[12] explains the lack of colloid in the follicles by the rapidity of its export. Ehrich, however, with right, suspects that the colloid-like substance in arteries and veins is merely the coagulated serum. Indeed he denies that any secretion escapes from the gland, and thinks the whole process a retrogressive one. Support is lent to Ehrich's views by the work of Oswald (*Virchow's Archiv*), who finds a decreased percentage of iodin in the thyroid in exophthalmic goitre, and considers the change a decrease in functional activity.

There is no statement in the literature as to any changes in the parathyroids in this affection, but an enlargement of the thymus is fairly constant, and in most of the cases a swelling of the cervical lymph glands has been observed. In a case recently dissected at the Johns Hopkins Hospital the hæmolymph glands in the neck were especially prominent.

The other organs show, as far as is known, no constant lesions. Askanazy has described certain degenerative changes in the voluntary muscle, but investigations confirmatory of his results seem not to have appeared.

Etiology.—Several distinct theories as to the etiology of the disease have been proposed, but they all fail to account satisfactorily for all the symptoms.

According to one, which has been defended by Buschan, exophthalmic goitre is a general neurosis in which the psychic and vaso-motor functions are predominantly affected; but constant changes in the thyroid cannot be explained on this idea.

Möbius is the chief defender of the theory of hyperthyroidization, in which the thyroid forms the starting-point for all the symptoms. Certain authors have shown that unpleasant symptoms—flushing, tachycardia, etc.—may follow the excessive administration of thyroid extract in normal animals, and it has been conceived that in this disease the enlarged thyroid is in a state of great secretory activity, pouring into the lymphatics far more of its secretion than normal, and thus bringing about the characteristic symptoms. This view seems further supported by the results of surgical extirpation of part of the gland—the relief of the symptoms being frequent. Not all the symptoms can be produced by injection of thyroid extract into normal animals, however, nor can all of the symptoms of exophthalmic goitre be relieved by extirpation of the active gland. For example, the exophthalmos can neither be produced by thyroid extract nor always relieved by thyroidectomy. There is much in favor of this theory, but also several arguments opposed to it are difficult to answer. The disease is considered to be a sort of general antithesis to the condition of myxœdema, which we know to be due to loss of the thyroid, and hence again the idea that such a reversal of the symptoms of myxœdema must be due to hyperthyroidization. But histologically we cannot say with certainty that the gland is secreting actively. Indeed, of the usual colloid we see little or nothing at all. The theory fails to explain several important symptoms. The results of the operation for extirpation of part of the gland are not uniformly good, and indeed not especially better than the rest in bed and regular régime alone; and finally cases of exophthalmic goitre in combination with myxœdema have been described—a condition which must directly contradict and disprove the theory of hyperthyroidization.

Ehrich thinks that the enlargement of the thyroid, and indeed most of the other symptoms, are due to the arterial hyperæmia, but he fails to explain this itself.

Mendel's theory of a lesion in the corpora restiformia falls on account of the inconstancy of such a lesion.

Finally, a theory has been based upon the effect upon the eyes of stimulation of the cervical sympathetic, ascribing the exophthalmic goitre, or at least many of its symptoms, to a lesion of the sympathetic. Now it was stated above that lesions of the sympathetic are by no means constant or even common, but the theory is not plausible upon the face of it for the following reasons: Section of the sympathetic causes pallor of that side of the face, retraction of the eye, and narrowing of the pupil, while stimulation causes a flushing of the face, sweating on that side, protrusion of the eyeball, widening of the palpebral fissure, and dilatation of the pupil. Those symptoms of exophthalmic goitre might therefore correspond with the results of a constant stimulation of the sympathetic, but even then the pupillary disturbances are absent in exophthalmic goitre, while they form the most striking consequence of stimulation of the nerve.

The nature of the exophthalmos has given rise to much discussion in this connection. It is by no means proven that it is due to distention of retrobulbar vessels; nor can it be shown that it is due to stimulation of the sympathetic, perhaps by pressure of the enlarged thyroid, for removal of the goitre influences it very little. Protrusion of the eyeball is, however, not impossible to the normal individual, and experiments of Filehne[13] and Durdufi[14] have shown that irritation of the corpus restiforme will produce exophthalmos even after the sympathetic is cut through. So also Kotschanowski[15] claims that it may be produced by stimulation of certain anteriorly placed cortical centres.

The theory of sympathetic irritation, being as it is without anatomical basis, explains only haltingly a few of the symptoms. It is impossible to make the lack of pupillary change agree with this conception, and the general tremors, general sweating, and vaso-motor disturbances, as well as the metabolic disorders and psychical symptoms, are not explained at all by such a theory.

Recent experimental work upon the thyroids and parathyroids seems to promise some light upon the subject. Briefly stated it has been found (Moussu,[16] Vassale and Generali,[17] Schiff,[18] and Gley[19]) that extirpation of the thyroids produces certain disturbances of nutrition which lead to the condition of myxœdema or cachexia strumipriva, while extirpation of the parathyroids leads, and in a far shorter time, to the death of the animal from symptoms of violent poisoning of the central nervous system—tetanic convulsions, dyspnœa, etc.—and that the tetany, which was previously ascribed to the removal of the thyroids, is really due to the simultaneous removal of the parathyroids, which are closely associated with them. Certain changes in the thyroid are said to occur after parathyroidectomy, and the tetany so produced is ameliorated by the removal or partial removal of the thyroids.

Slight exophthalmos sometimes occurs in the animals from which the parathyroids have been removed, and altogether the symptoms are rather suggestive of those of exophthalmic goitre. The suggestion has therefore been made (Gley, *British Med. Jour.*, 1901, September 21st), and is now being put to the proof, that possibly the development of this disease depends upon some lesion which destroys the parathyroids, and that it is nothing more than a long-continued parathyroid insufficiency. Indeed, one promising but incomplete attempt at the relief of the symptoms by parathyroid therapy has been made by Moussu.[20] As stated above, there appears to be but a very meagre description of the parathyroids in exophthalmic goitre in the literature (Benjamin's, "Ziegler's Beiträge," Bd. xxxi.), but in several cases which have recently occurred in the Johns Hopkins Hospital it was found possible to isolate parathyroids in four, although the glands were small, degenerated, and sclerotic. In a fifth and fatal case no parathyroid tissue was found at autopsy. It can readily be understood on this theory that the cases of combined myxœdema and exophthalmic goitre offer no difficulties. They are readily explained as cases in which the destruction of the thyroid produces the myxœdema, while destruction of the parathyroid independently produces the exophthalmic symptoms.

The theories as to the etiology are thus as yet not entirely satisfactory, although the last mentioned seems at least to offer some promise.

Course of the Disease; Prognosis; Treatment.—The disease runs sometimes a very rapid course, terminating fatally after an illness of a few days only. In most instances it drags on for years and may end in recovery. The prognosis indeed is by no means very unfavorable, and a considerable proportion of the cases get quite well. There have been cases reported in which some sudden emotional shock is followed by intense symptoms, such as have been described, which after a short time disappear completely. In the cases in which the most intense symptoms are developed, however, and in which the clinical picture is complete, recovery without surgical interference is rare. The greatest variety of procedures has been employed in the attempt to cure these cases. From the medical point of view none are very satisfactory. Rest in bed, freedom from emotional disturbances, and the regular régime of the hospital seem to afford great relief in many cases, and are extremely important in the cure. The tachycardia is apparently not influenced by digitalis, although strophanthus is said

to have some effect. Ergot and belladonna have been warmly recommended by some authors, and may do some good. Electricity, too, applied to the spine and peripheral nerves has been advocated by Erb and others.

Based on the remarkable results obtained by the administration of the thyroid gland in myxœdema numerous cases of exophthalmic goitre have also been treated in this way regardless of the theory of hyperthyroidization, but the effects have been either actually harmful or entirely negative. The cases in which thyroid therapy has produced untoward results have therefore been brought forward as a strong support of the idea that the thyroid is already secreting too profusely, and thereby causing the symptoms.

From the fact that the thymus is usually found enlarged in exophthalmic goitre extracts of thymus have been given in these cases, sometimes with remarkable temporary results, but without any permanent advantage to the patient. In the case referred to above, which occurred in the Johns Hopkins Hospital, administration of the thymus extract reduced the pulse rate at once from 200 per minute to normal. When it was discontinued the pulse rose again to 200, and was again brought to normal by the thymus extract. After a time, however, its effect disappeared, and the pulse rate remained high until the death of the patient. In another case there occurred a remarkable reduction in the size of the goitre during its use. Since the parathyroid lies embedded in the thymus in the ox and certain other animals, it seems possible that it may be included in the extract manufactured from the thymus of these animals and may be responsible for the above results.

It was stated above that one attempt has been made to influence the symptoms by parathyroid feeding, and indeed the great amelioration following its use seemed very promising. The patient, however, died of tuberculosis before any definite result was attained. It is quite difficult to procure the glands in sufficient quantity for such treatment, but as soon as a parathyroid extract is on the market, it will be possible to give this remedy a thorough trial.

Quite recently Lanz,[25] Möbius,[21] Goebel,[22] Schultes,[23] and others have proposed and carried out a treatment which is based on other principles, and which they claim to be very successful. On the idea that the thyroid is concerned in the neutralization of poisons produced elsewhere in the body, and that in exophthalmic goitre it is so active that not only does it neutralize these poisons but further poisons the organism by the excess of this antitoxin (!), these authors attempt to supply this overactive thyroid with poison for neutralization by injecting the serum of thyroidectomized sheep, in which supposedly much of the poison must have accumulated, or by feeding them on the milk of such thyroidectomized animals. The chances for fundamental error in the conception of this treatment seem very great, for it is by no means proven that in exophthalmic goitre the thyroid is overactive; nor, on the other hand, is it proven that the function of the thyroid lies in the neutralization of poisons elaborated elsewhere.

In recent years the surgical treatment of exophthalmic goitre has become very prominent. It also is based upon the idea that the enlarged thyroid is overactive in pouring its secretion into the lymphatics, and the cases are therefore subjected to the partial extirpation of the thyroid.

The operation is a serious one, hemorrhage being very difficult to control. The patients do not take the anæsthetic well and many have died on the table.

Of late years, however, many of these operations have been performed under a local anæsthetic. Kocher[24] has reported fifty-nine cases, in which the results have been on the whole very satisfactory, often with almost complete or complete relief of all the symptoms. Usually the exophthalmos persists or disappears gradually, and often the improvement in the symptoms does not immediately follow the operation, but appears later. Much anxiety has been expressed from time to time as to the dangers of allowing the escape of thyroid secretion into the wound during such an operation, and the fever which sometimes follows the operations has been ascribed to this. Lanz,[25] however, has shown experimentally that the most violent crushing and laceration of the thyroid which is then left *in situ* is not usually followed by any rise in temperature nor by any special untoward symptoms.

Ehrich has reported eight cases of operative extirpation of part of the thyroid in exophthalmic goitre, but is far less enthusiastic about the results. Many of these were not relieved, or suffered a recurrence of all the old symptoms after a temporary relief. He thinks that on the whole the good results are due mainly to the regular régime of the hospital for a time after the operation and to the suggestive effect of the operation.

In some instances merely ligation of the vessels of the thyroid has been performed, often with favorable results.

In none of these operations has any attention been paid to the condition of the parathyroids.

Operations for the section or removal of the cervical sympathetic trunks have been performed (Jaboulay,[26] Balacescu[27]), with results which they claim to be quite as good as those obtained by the extirpation of the thyroid.

A definite opinion as to the value of these different methods of treatment must, however, be reserved until our knowledge of the results is more extended.

William G. MacCallum.

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EYEBALL, ENUCLEATION AND EVISCERATION OF.—I. ENUCLEATION.—By enucleation is meant a shelling of the eyeball out of Tenon's capsule with preservation of the relation between the conjunctiva, ocular tendons, and the other contents of the orbit.

History.—In 1841 Bonnet, of Lyons, first described and recommended true enucleation. The operation had been performed in a very crude manner by Bartisch, of Saxony, in 1583, by passing a sharp spoon behind the eyeball and thus gouging it out of Tenon's capsule. Bonnet's operation had the great merit of preserving the capsule of Tenon and disturbing as little as possible the soft parts of the orbit. It became justly popular. Like most surgical procedures it has been variously modified by different operators. During the past few years it has been greatly improved and its cosmetic effect enhanced by suturing the tendons of the four straight muscles to the conjunctiva.

Operation.—The following instruments are required: A stop speculum, fixation forceps, toothed forceps, strabismus scissors, strabismus hook, a strong pair of scissors curved on the flat for cutting the optic nerve, a needle-holder, fine curved needles, and black silk for sutures. A general anæsthetic is advisable, although the operation may be performed under local anæsthesia.

The lids being held apart with a stop speculum, the surgeon incises, with strabismus scissors, the conjunctiva and adjacent fascia all around as close as possible to the corneal margin, and dissects the same from the sclerotic as far as the insertions of the tendons of the straight muscles. The tendon of each straight muscle, beginning with the internal rectus, is then, in succession, raised upon a strabismus hook and secured with a suture of black silk, after which the tendon is severed with strabismus scissors as close to the eyeball as possible. The anterior portion of the eyeball being now free from all attachments, may be dislocated forward by pressing the stop speculum back. The curved enucleation scissors are next introduced with the points closed and are pushed backward between the eyeball and the detached conjunctiva until the optic nerve is felt. After the exact position of the optic nerve is found, it is included between the blades and cut close to the sclerotic by one strong cut. The eyeball now readily protrudes and is held by the fingers of the left hand, while the tendons of the two oblique muscles and all adherent tissue are severed close to the globe. A small ball of sterilized gauze is inserted in the capsule of Tenon for the purpose of checking hemorrhage and of aiding the next step, the suturing of the tendons of the straight muscles to prevent their retraction. Each rectus tendon is now drawn forward and fastened to the margin of the conjunctiva by the same suture which was inserted just before the division of the tendon. The sterile gauze should now be removed, the margins of the conjunctiva and capsule of Tenon united with several interrupted sutures, and a dry antiseptic dressing applied. Both eyes should be bandaged for twenty-four hours and the patient kept in bed for a couple of days. The socket should be washed out once daily with physiologic salt solution until after four or five days, when all dressings may be discontinued.

The technique of the operation, as above described, has been varied by different operators. The most important variations relate to methods of preparing the stump after enucleation, which will best secure motility of the prothesis and furnish cosmetic results. The following method has been brought forward by G. F. Suker: After removing the eye, the severed tendons of the recti muscles are brought together by means of the silk guides and sutured one to the other with either catgut or silk. The conjunctiva from above and below is then brought over the muscle stump and sutured with a continuous or interrupted suture. H. V. Wurdemann, who was one of the first ophthalmologists to point out the advantages of a properly prepared stump, makes a pouch suture by weaving the needle along the cut edges of the divided conjunctiva and Tenon's capsule. In passing the recti tendons, each one is picked up on the needle.

H. Schmidt has suggested the following method: Each tendon of the recti muscles is secured by a catgut suture, and, after division, is fastened to a slit made in the conjunctiva over the site of the tendon's insertion. The opposite edges of the conjunctiva are then brought together with a continuous suture.

Priestley Smith has described the following method of suturing the tendons to the conjunctiva: A narrow horizontal fold of the conjunctiva over the internal rectus is pinched up so as to include the subjacent connective tissue and muscle, and a black silk thread is carried through these structures by means or a curved needle. The suture is then tied firmly but not too tightly. A second suture is applied in like manner to the external rectus. The upper and lower recti may be treated in the same way, but this is of less importance. The enucleation is then carried out and the conjunctival aperture may or may not be closed by one or more vertical sutures.

Complications and Accidents.—Hemorrhage occasionally severe and persistent, may occur during the operation or later. In enucleating an inflamed eye, there is always a good deal of hemorrhage, particularly where there has been extension of inflammation into the surrounding tissue. The hemorrhage in this case is beneficial. Hemorrhages following an enucleation may require repeated packing of the orbit with antiseptic gauze. Occasionally a secondary hemorrhage occurs, when the dressings must be removed and the orbit packed with gauze. In these cases the tissues of the orbit may become greatly swollen from infiltration with blood. In chronically inflamed eyes, dense adhesions, binding the conjunctiva and its underlying fascia to the sclerotic and the tendons of the straight muscles, may be encountered. These cases often require a most careful dissection in order to expose the tendons, but by taking time and keeping the sclerotic always before him, the surgeon may perform the operation without accident. In enucleating an eyeball that has been perforated, or one soft from any cause, great care must be taken to remove it without leaving portions of the sclera and choroid behind. When an eyeball is enucleated because it contains a malignant growth, the posterior orbit should be carefully explored with the finger and probe before severing the optic nerve; and if a tumor is found, it should be removed along with the eyeball. As much of the optic nerve as possible should be removed with the globe. In very rare cases, enucleation has been followed by fatal meningitis, especially when performed on an eye within which suppuration was taking place. Up to 1900 G. E. de Schweinitz had collected fifty-two cases of fatal meningitis following enucleation, "thirty-three of which certainly—and a larger number probably—had followed enucleation for one stage or another of suppurative disease within the globe." The risk of a fatal termination from any cause after enucleation is about one in sixteen hundred. Meningitis after enucleation of a non-suppurating eyeball is exceedingly rare. In 1898 the Committee of the Ophthalmological Society of the United Kingdom could not find a single instance among 10,734 cases gathered from various sources.

Indications for Enucleation.—There are certain affections of the eye for the relief of which enucleation is demanded and cannot be replaced by any other operation. Enucleation is demanded in all cases of malignant tumor of the globe except in those rare cases of tumors which grow at the limbus and on the conjunctiva or iris. It is also required in cases of malignant tumors of the orbit which cannot be removed without sacrificing the eye. Enucleation is to be performed in those cases of sympathetic ophthalmitis in which the sight of the exciting eye has been lost. It is also demanded in the cases of eyes so injured that they are likely to excite sympathetic ophthalmitis, if two weeks or more have elapsed since the injury; for while enucleation cannot prevent all cases of sympathetic ophthalmitis, it is the operation which holds out the best chance for the prevention of the disease.

On this account enucleation should be performed in the case of an eye with a wound so situated as to involve the ciliary region, and so extensive as to have destroyed the sight or to make its ultimate destruction by iridocyclitis reasonably certain. It is also indicated in the case of an eye with a wound in the ciliary region, complicated by severe inflammation of the iris or ciliary body, even if sight is not destroyed; or of an eye containing a foreign body, which judicious efforts have failed to extract, and in which severe iritis is present, even if sight is not destroyed. Enucleation is also to be performed in the case of an eye in which the wound has involved the cornea, iris, or ciliary region, and in which persistent sympathetic irritation in the fellow-eye has occurred, or in which there have been repeated relapses of sympathetic irritation; in the case of an eye long blind from injury which has become red and painful; in cases of painful phthisis bulbi, and in those in which the choroid has undergone calcareous changes. Enucleation is also indicated

in cases of grave traumatisms in which the sclerotic coat is extensively lacerated.

Other affections, believed by many surgeons to require enucleation, but for which one of its substitutes may be performed, are: Eyes so injured that they are likely to excite inflammation, which have come under observation within two weeks from the time of injury; painful glaucomatous eyes, unrelieved by sclerotomy; chronic painful iridocyclitis; panophthalmitis without involvement of the orbital tissues. In extreme old age enucleation is to be preferred on account of the recovery being smoother and shorter than is usually the case in evisceration. The same consideration may decide both the surgeon and the patient in favor of enucleation in the case of a workingman, especially where the cosmetic results are not important.

The Relation of Simple Enucleation to the Wearing of an Artificial Eye.—The artificial eye may be fitted as soon as the wound is entirely healed, in the second or third week. The following rules have been adopted by the Moorfield Ophthalmic Hospital, London, for the guidance of patients wearing artificial eyes.

To put the eye in: Place the left hand flat upon the forehead, and with the two middle fingers raise the upper lid toward the eyebrow; then, with the right hand, push the upper edge of the artificial eye beneath the upper lid, which may be allowed to drop upon the eye. The eye must then be supported with the middle fingers of the left hand while the lower eyelid is raised over its lower edge with the right hand.

To take the eye out: The lower lid must be drawn downward with the middle finger of the left hand; and then, with the right hand, the end of a small pin must be put beneath the lower edge of the artificial eye, which must be raised gently forward over the lower lid when it will readily drop out.

Patients very soon become expert in introducing or taking out artifiical eyes and do not require the aid of a pin in removing them. The artificial eye must be removed every night and carefully cleansed. In selecting an artificial eye for use after enucleation the various forms of glass eye, proposed by Snellen, are decidedly superior to the older form of a simple shell. The cosmetic effect of the Snellen reformed eye after a well-performed enucleation is so good that many surgeons believe that it renders unnecessary the operations which have been brought forward as substitutes for enucleation.

Implantation of an Artificial Globe in Tenon's Capsule after Enucleation (Frost-Lang Operation).—The eyeball is enucleated in the ordinary manner, and after all hemorrhage has been arrested an artificial sphere is inserted within Tenon's capsule for the purpose of forming a more prominent stump and giving it greater activity and mobility. Glass and gold spheres are commonly employed, more rarely celluloid or silver balls. Sterilized paraffin injected into Tenon's capsule has been advocated by Ramsay and Oatman. The capsule and conjunctiva are sutured over the artificial ball with silk sutures, the tendons of the straight muscles having first been secured in the manner described under enucleation. The following method of performing the operation has been introduced by C. A. Oliver: "The conjunctiva around the entire corneal limbus is freed from the globe and dissected sufficiently far back so as to expose the tendons of the four recti muscles. The tendinous extremities of the muscles are made ready for separation from the globe. A half-curved needle with its point directed toward the corneal border and holding a long piece of catgut thread is carried directly through the belly of the internal or the external rectus muscle and brought out of the tendon of the muscle just behind the remaining attachment to the globe. The muscle thus secured is cut loose from the globe just as in ordinary tenotomy. The catgut thread is drawn through as far as practicable, and a sufficient length of the strand of gut is left untouched to allow a loop broad enough for free manipulation between it and the eyeball. The needle is carried over to the opposite side of the cornea, and with its point directed away from the cornea is made to transfix the tendinous belly of the other lateral muscle, which is secured and freed from its attachment to the eyeball. The vertically placed muscles are dealt with in a similar manner. The four recti muscles are thus freed from their attachments to the globe, and each pair of muscles secured by a loose sling, that can be tied the moment this becomes necessary. Working in between the broad loops of catgut, attached to the ends of the muscles that are held apart by an assistant, the eyeball is enucleated The cavity previously occupied by the globe is thoroughly cleansed and a water-tight glass ball, about three fourths the size of the normal eye, is dropped into place. The ends of the lateral recti muscles, which are held by the lower and first-placed thread, are neatly trimmed and sutured together. The same is done with the two ends of the vertical straight muscles. The circular opening made by the cut edges of the conjunctiva is made into a lozenge by a couple of horizontal snips, and is carefully brought into linear apposition by a series of silk threads. The operative field is covered by a gauze protective bandage upon which ice compresses are placed."

Indications and Contraindications.—An artificial globe may be implanted in Tenon's capsule whenever it is necessary to remove the eyeball completely, except in cases of malignant disease, sympathetic ophthalmitis, suppuration within the globe, and in extreme old age.

Complications.—These are: Hemorrhage, orbital cellulitis, sympathetic irritation, tearing out of the stitches from sloughing with escape of the artificial ball, and late cicatricial contraction of the orbital tissues, causing extrusion of the ball. Adolph Bronner has lately advocated the insertion of a glass ball with a hole through the middle, which is covered in with glass so as to keep the ball air- and water-tight. By a somewhat elaborate method of stitches, this is held in, and he claims is less liable to be thrown off than a simple globe.

After-Treatment.—The eye should be dressed with a dry antiseptic dressing and both eyes bandaged. Care should be taken to avoid using pressure bandages. If much reaction follows, it is advisable to employ an ice bag for the first twenty-four hours. The patient should be confined to bed for four or five days.

An artificial shell—the ordinary or Snellen's—can be inserted at the expiration of a month or six weeks. The cosmetic result is apparently no better than that which is obtained by a properly performed enucleation and the wearing of a Snellen reformed eye.

Implantation of a Piece of Sponge in the Orbit after Enucleation.—This procedure has been suggested by Claiborne, of New York, and Belt, of Washington, for the purpose of gaining a more prominent stump and an improvement in adapting prothesis. The method has never come into general use on account of the prolonged convalescence and the late results being no better than those of a well-performed enucleation.

II. Evisceration.—In this operation the cornea and entire contents of the eyeball are removed, the sclera alone remaining. This procedure was first proposed by Alfred Graefe, in 1884, to prevent meningitis after the removal of eyes affected with panophthalmitis.

The instruments required are eye speculum, fixation forceps, a Graefe or Beer knife, strabismus scissors, sharp spoon, needle-holder, small curved needles, catgut and silk sutures.

Operation.—After general anæsthesia the speculum is introduced and the eyeball steadied by grasping with fixation forceps a fold of conjunctiva near the corneal margin. The eye is then transfixed just back of the corneal limbus with a Beer or Graefe cataract knife, which is made to cut its way out at the upper or lower sclerocorneal border, so as to include the corneal and about 1 mm. of the scleral margin in the flap. The flap is now grasped with forceps and the remainder of the incision completed with scissors. The next step is to remove the entire contents of the sclera, great care being taken that nothing is left behind, especially none of the choroidal

tissue The wound being kept open by two pairs of forceps, a sharp spoon-shaped instrument, grasping its edges about 10 mm. apart, is pushed between the choroid and sclerotic and carried sideways and deeper in order to detach the whole contents of the sclerotic, if possible unbroken.

It is usually impossible to eviscerate the contents of the globe as a whole. They must be removed with gauze sponges grasped by forceps, which are given a rotary movement, until, by scraping and wiping, the inner surface of the sclera is made perfectly clean. After hemorrhage has been controlled, the cavity should be irrigated with physiologic salt solution and the edges of the sclera and conjunctiva brought together by interrupted silk sutures. If preferred, the edges may be united by means of a suture similar to the gathering string which draws shut a tobacco pouch—a suture sometimes called the tobacco-pouch suture, or the purse-string suture.

Gifford, of Omaha, whose experience in evisceration has been unusually large, covering over one hundred cases, has devised the following method of operating: A large conjunctival flap is first turned back and a long meridional incision made through the sclera Evisceration is performed through this opening, leaving the cornea intact. Gifford claims that the reaction is less and the stump better than when the cornea is excised. The latter shrinks to a mere patch on the anterior surface of the stump.

The dressing after evisceration should be a light, dry, antiseptic one. The patient should remain in bed at least four or five days with both eyes bandaged. Cold applications should be used for a day or two to keep down the reaction. The sutures may be removed in from three to four days. The recovery is commonly less smooth than that from simple enucleation, and considerable pain with œdema and swelling of the surrounding tissues may follow the operation. The operation is often performed when the inflammatory process is already high, and when the orbital tissues are secondarily involved. No cases of meningitis have occurred. Sloughing of the sclera has been noted, and a painful stump may be one of the complications.

Indications for Evisceration.—The operation having been introduced by Alfred Graefe as a substitute for enucleation in cases of panophthalmitis, it very naturally followed that this affection at once took front rank as an indication for evisceration. Graefe had lost two patients in 1863 from meningitis following enucleation, and almost all surgeons in Germany, where his influence was supreme, feared to enucleate an eye during the height of panophthalmitis. Mauthner tells us that this feeling went so far that a German operator even excused himself for having enucleated two panophthalmitic eyes with the best results, because he did not know at the time what Graefe had said on this point. Writing in 1878, Mauthner graphically describes his own feelings on the subject. "Personally," he says, "I stand in awe of Graefe's advice never to operate if the panophthalmitis is distinctly pronounced. I have never enucleated an eye under such circumstances, and I doubt if I shall ever make up my mind to do so. The terrible apparition in von Graefe's cases impresses me so deeply that at the very sight of an eye in a state of panophthalmitis, and the thought of enucleating it, the dread of a fatal result is conjured up before me."

Notwithstanding his fears, Mauthner apparently had very grave doubts regarding the justifiability of abstaining from operation, and allowing suppuration within the eyeball to continue without interference. Meantime, the English oculists, under the leadership of Critchett, continued to enucleate during panophthalmitis as complacently as though Graefe had never warned against it, and Gunn, discussing a fatal case reported by Nettleship in 1886, said that this was the first fatal occurrence among over a thousand enucleations done at Moorfield Ophthalmic Hospital. American ophthalmologists have never paid much attention to panophthalmitis as a contraindication for enucleation, and Noyes, in a paper read before the American Ophthalmological Society in 1889, on "Enucleation during Panophthalmitis," says: "We are certainly justified in performing the operation notwithstanding the warnings and alarming declarations of Prof. Alfred Graefe."

Although the risk of a fatal termination after enucleation during panophthalmitis is so small that the operation may be performed almost with impunity, there can be no doubt that when the purulent inflammation has extended to the orbital tissues evisceration is the safer plan. Staphylomas of the cornea, especially when they occur in children, are well suited to evisceration. Painful, blind, glaucomatous eyes, or eyes blind from chronic, non-traumatic iridocyclitis, may also be safely eviscerated. This operation will also be indicated in the cases of eyes injured in the anterior portion of the globe, when all thought of recovery under conservative treatment has been abandoned within two weeks of the time of injury.

Contraindications.—These are malignant disease, sympathetic inflammation, sympathetic irritation, phthisis bulbi, ossified choroid, and foreign bodies penetrating the orbit.

The Relation of Simple Evisceration to the Wearing of an Artificial Eye.—A Snellen artificial eye may be inserted during the third or fourth week. The ultimate cosmetic effect is no better than, and in some cases not so good as, that obtained after enucleation performed according to modern technique.

Evisceration of the Eyeball, with Insertion of an Artificial Vitreous; Mules' Operation.—Mr. Mules, of Manchester, England, in 1886, modified the operation of simple evisceration by the introduction of a glass ball into the cavity of the sclera. The operation is performed as follows: After general anæsthesia a stop speculum is introduced and the conjunctiva freed all around from the corneal margin and dissected back as far as the equator of the eyeball, without disturbing the relations of the muscles. The cornea and 1 mm. of the scleral margin are then removed in the manner described under evisceration. A triangular portion of the sclera, above and below, should also be removed to facilitate the introduction of the artificial vitreous, and in order that the coaptation of scleral edges over the same may be perfect. Next, the contents of the globe should be removed in the manner described under simple evisceration, and all hemorrhage arrested by packing the scleral cavity with dry sterile gauze, or gauze soaked in hot sterile water. The next step is the introduction of a thoroughly sterilized artificial vitreous, usually of glass or gold. A sphere of such size that it can be easily inserted within the scleral cavity is selected. The introduction of the sphere is best effected by means of a special instrument designed for the purpose by Mr. Mules. The margins of the scleral opening are then united vertically by means of interrupted silk sutures, and the conjunctival opening is closed by another line of sutures placed at right angles to the sclerotic line of closure. The greatest care must be observed to secure absolute asepsis during the operation and at all subsequent dressings. A bandage which does not make much pressure should be adjusted over a dry antiseptic dressing. The fellow-eye should also be bandaged and, unless for special indications, the dressing should not be removed for forty-eight hours. Should there be decided reaction, iced compresses should be applied. The patient should be kept in bed for three or four days and both eyes bandaged until there is firm union of the wound. The superficial sutures should be removed on the third day, the scleral suture remaining permanently.

Some surgeons perform the operation according to a different technique from that described above. Gifford eviscerates through a horizontal incision in the sclerotic according to his special method previously described, and implants the artificial globe through this opening without removing the cornea. Some operators close the sclerotic and conjunctival wounds with the same sutures.

The purse-string suture is used by some of the best operators for closing the scleral opening, after which the conjunctival wound is closed with another purse-string suture. Some operators advise the removal of the conjunctival suture at the end of forty-eight hours. Mr. Collins, of Moorfield Hospital, believes that many failures of this operation are due to allowing the superficial suture to remain too long.

Indications.—The chief indications for this operation, as given by de Schweinitz, are: Staphyloma of the cornea and sclera, ruptured or injured eyeballs when the sclera is not too much lacerated and when the accident is of recent date, absolute glaucoma, buphthalmos and non-traumatic iridocyclitis.

Contraindications.—The following contraindications are enumerated by the same authority: Suppuration of the eyeball; morbid growths; much shrunken eyeballs, the contents of which have undergone bony or calcareous change; sympathetic ophthalmitis; sympathetic irritation and pathologic conditions of the eyeball which are likely to produce either of the last-named affections; extensive injuries of the eyeball, with much bruising and laceration of the sclera; dacryocystitis and ocular conditions demanding enucleation or its equivalent in very old persons.

Accidents and Complications.—The operation may be followed by excessive reaction manifested by marked swelling of the lids and chemosis of the conjunctiva, headache, nausea and vomiting, and elevation of temperature. It is probably always caused by faulty technique, as imperfect asepsis, failure to arrest hemorrhage, the use of strong antiseptics and undue dragging upon the optic nerve. Sloughing of the sclera and consequent cutting out of the stitches occur in about eight per cent. of all cases. Extrusion of the artificial vitreous within the first week or at a much later period took place in seventeen per cent. of the three hundred and sixteen cases in the hands of thirty-three different operators, tabulated by de Schweinitz. The chief cause of escape of the artificial globe is failure of the edges of the scleral wound to unite. Another important cause of the throwing-out of the glass ball is that it may have been too large or too small for the scleral cup. An irritable and painful stump requiring removal has been met with as a complication following the operation. Sympathetic inflammation has been met with as an unfortunate complication in a number of instances. While in most cases it was due to the seeds of the disease having been planted before this operation was performed, it seems in several instances, as in the case reported by Carrow, to have been directly due to the operation itself. The report of the committee of the Ophthalmological Society of the United Kingdom in 1898 contains the following statements: "We have not found a record of any case of sympathetic ophthalmitis following evisceration without the implantation of an artificial globe, and we have collected records of five cases of sympathetic ophthalmitis after the operation of evisceration and the introduction of an artificial globe into the emptied sclerotic." Sympathetic irritation has been met with on rare occasions and required the removal of the stump.

Special Advantages with Relation to the Wearing of an Artificial Eye.—After a successful Mules' operation the motility of the stump and artificial eye is usually better than that after enucleation, the implantation of a ball in Tenon's capsule, or simple evisceration. The cosmetic result is extremely satisfactory, for the natural contour of the lids being preserved, there is none of the shrunken appearance so often presented by artificial eyes. The absence of accumulations of mucus and tears adds to the patient's comfort and satisfaction. The high percentage of failures, due to extrusion of the artificial vitreous, must be greatly reduced before the operation can take a permanent place in ophthalmic surgery. At the present time the prevalent feeling among ophthalmologists regarding the operation of Mules is one of disappointment.

Edmund W. Stevens.

FACIAL HEMIATROPHY.—(Synonyms: Unilateral atrophy of the face; Progressive facial hemiatrophy; Progressive laminar aplasia; Facial trophoneurosis; Facial circumscribed atrophy.)

The first known description of facial hemiatrophy is that by Parry, written in 1825. In the year 1846 Romberg described the condition more definitely and called it a trophoneurosis.

The disease consists of an acquired circumscribed atrophy of the face. The atrophy, involving soft tissues and bone, follows a chronic course, and finally becomes spontaneously stationary.

Something over one hundred authentic cases have been reported.

Etiology.—The disease belongs to the period of youth. Practically all of the reported cases began before the thirtieth year. Women are more frequently affected than men, in the proportion of about two to one. It does not appear that nationality, station in life, or heredity has any influence on the development of the syndrome. In the reported cases it has followed typhoid fever, measles, scarlet fever, syphilis, and other infectious diseases. It has been observed in the course of multiple sclerosis, syringomyelia, multiple exostoses of the face and head, scleroderma, insanity, epilepsy, and hysteria. It is not unusual for the patient to ascribe it to blows or other injuries to the face. In a number of cases the early symptoms have been those of a severe trigeminal neuralgia. In one case which I saw there had been a severe malarial infection one year before.

Pathological Anatomy.—Various theories have been advanced in regard to the lesions which may produce facial hemiatrophy. Disease of the sympathetic nerves, of the peripheral distribution of the fifth cranial nerve, of the Gasserian ganglion, of the nuclei of the fifth nerve, and of the cortex of the cerebrum have in turn had their theoretical advocates. The principal anatomical evidence rests on the findings in Mendel's case; this was a woman who for fifteen years had suffered from left facial hemiatrophy. The autopsy showed the epidermis normal except for a moderate degree of thinning, the connective tissue was diminished, the blood-

Fig. 5137.—Facial Hemiatrophy Beginning in a Woman Twenty-four Years Old. (After Fromhold-Treu.)

vessels were few and small, the fibres of the muscles were somewhat thinned without degeneration or nuclear changes, and the facial nerve was normal. In the trigeminus the connective tissue around and penetrating the nerve was much thickened. In many places the number of nerve

fibres was diminished. Most of the changes were in the second division of the nerve. There was also atrophy of the descending root of the trigeminus and of the substantia ferruginea. Mendel believed that the facial atrophy was due to the proliferative interstitial neuritis of the trigeminus. In this case there was also an atrophy affecting the left upper extremity and some of the muscles of the shoulder and back. To account for this Mendel found an interstitial neuritis of the musculo-spiral nerve and a diminution in size and number of the cells of the anterior horn of the cord at the level of the fifth cervical nerve.

The antecedent neuralgias of the fifth nerve point to this as the site of the lesion. But how many severe neuralgias of this nerve have we not seen with no subsequent atrophy? Section of the posterior root of the trigeminus may be attended by unilateral atrophy of the muscles of the face, tongue, and bones of the face, and changes in the amount and color of the hair. Operations on the Gasserian ganglion have been said to be unattended by trophic changes in the skin.

Other autopsies in patients showing facial atrophy have shown other lesions which take them out of the group of cases now under discussion. Such was Graff's case, which showed on autopsy a progressive muscular atrophy, and that of Jolly and Recklinghausen, in which was found a disseminated sclerosis of the brain.

Symptoms.—Patients who develop facial hemiatrophy usually present themselves to the physician complaining of a neuralgia in the distribution of the trigeminal nerve. After this has lasted for several weeks or months the cardinal symptom of the syndrome appears. This consists in an atrophy commencing in the skin of the face. There appears on the face a whitish spot which may soon be followed by other similar spots. These may extend until they cover half of the face, or may be limited to a small area. Gradually these areas change in color to a yellowish-brown, while the skin becomes thin and tightly stretched over the subcutaneous tissues. The extent of the atrophy may vary to a considerable degree. Fromhold-Treu indicates the varieties in his attempt to classify them: (*a*) Typical cases involving one-half of the face. (*b*) Incomplete cases involving a portion of one side of the face. (*c*) Double cases involving both sides of the face. (*d*) Cases in which other parts of the same side of the body are involved. Following the atrophy of the skin there is a falling away of the underlying tissues. The fat may totally disappear, but at times is said to be replaced after the atrophic process has come to a standstill. The frontal, malar, upper and lower jaw bones may atrophy. The muscles supplied by the fifth nerve become very thin, but their electrical reactions remain normal and their function is not wholly destroyed, though much weakened. The nasal cartilages usually waste; less frequently the auricle is involved. The hair of the head, eyebrow, and beard may change color, become thin, or fall out altogether on the affected side. The glands of the skin are usually unaffected, but anidrosis has been noted as well as diminished lachrymal secretion. The blood-vessels may show through the attenuated skin, marking it with an underlying network. The tongue and gums are frequently atrophied on the affected side. The tightening of the skin may interfere with the movements of the jaw. In the one case which I have observed the mouth was drawn to the normal side by the overaction of the healthy muscles. Taste, touch, and the electrical reaction are usually normal, even in the wasted half of the tongue. The trigeminal pain is occasionally associated with spasmodic contractions of the muscles, or with fibrillary twitchings. As the atrophy advances the pain usually subsides. There may be paræsthesias or spots of hyperæsthesia (probably due to thinning of the skin). Anæsthesia and changes in the temperature sense are exceedingly rare. The muscles supplied by the seventh nerve are usually unaffected. Mills reports a case in which the hearing was affected, probably on account of an atrophy of the tympanum. The pupil may be contracted; or, as in Mailhouse's case, may be dilated and fail to react to light or accommodation. The eyeball on the affected side appears prominent on account of the atrophy of the surrounding tissues.

Course and Prognosis.—The disease is insidious in its origin and slow in its development. It may continue to advance for two or three years, but all the cases ter-

Fig. 538.—Facial Hemiatrophy Following Pneumonia in a Woman Nineteen Years Old. (After Möbius.)

minate spontaneously, the majority at the end of one year, leaving an area of atrophy from which recovery is unknown. At the beginning one cannot predict the extent or duration of the atrophic process; it may involve a narrow furrow only, or half of the face, or even both sides of the face. As a rule a long and severe antecedent neuralgia suggests a less favorable prognosis. A cure or even an improvement in the atrophied parts is almost unknown, though some competent observers have claimed that in a few cases the face has filled out to a moderate degree; this was probably due to an increase in the fat. To the patient, however, cessation of the pain and muscular cramps is an improvement.

Diagnosis as a rule is not difficult. The points particularly to be borne in mind are that the disease is an acquired one, developing before the thirtieth year. There is a change in the color of the skin followed by atrophy; the muscles usually affected are those supplied by the fifth nerve. Congenital asymmetry and forms of degeneracy should be easily differentiated. Confusion in cases of hemiplegia and the malnutrition of sympathetic paralysis is hardly possible. In Bell's palsy the muscles supplied by the seventh nerve only are affected. In these muscles there is a reaction of degeneration to the electric current, and tissues other than muscular are not involved. In the type of progressive muscular atrophy which first involves the face, the muscles alone atrophy; the skin, connective tissue, and bone are not affected. This disease, moreover, is progressive, and later other parts of the body are involved. Atypical cases of scleroderma may be confounded with facial hemiatrophy. The skin of scleroderma is usually harsh and infiltrated, while that of facial hemiatrophy is thinned.

Treatment.—At the present time we know of no measure that will limit the course of the disease. Neuralgias following abscesses of the teeth, tonsillitis and the infectious diseases should receive careful attention. Electricity and massage appear to have no influence on the course of the disease or in restoring the atrophied tissues. No drugs which have been tried have been proved of benefit excepting in so far that they control the neuralgic pains and muscular spasm. Sachs suggests thyroid extract. The value of this, as far as I know, has

not been demonstrated. Section of the trigeminus, on the theory that the nerve stimulus is perverted, should be considered. Various contrivances have been devised for correcting the resulting deformity. Sachs has used a pad or rubber plate in the mouth. Eckstein has improved the appearance with subcutaneous injections of paraffin. *T. Stuart Hart.*

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Mobius: Der unsichtbare Gesichtsschwund. Nothnagel's Spec. Path. u. Ther., xi., 2, 1895.
Eckstein: Berl. klin. Woch., xl., p. 530, 1903.

FACIAL HEMIHYPERTROPHY is a rare affection consisting of circumscribed enlargement of one side of the face. The process usually involves the skin, connective tissue, blood-vessels, muscles, and bone. In some cases

Fig. 5139.—Facial Hemihypertrophy in a Child. (After Sabrazès and Cabannes.)

the skin is harsh and rough, while the sebaceous glands are much hypertrophied and clogged with an abnormally thickened secretion of gummy consistence. The hair is often thick and coarse. In the case reported by Dana the bones were alone involved in the process; the soft tissues were not hypertrophied. The external ear may take part in the enlargement. Here either the cartilage alone or all the tissues may be involved. The hypertrophy may extend into the mouth implicating the gums, soft palate, and jaw. The hypertrophy may be limited to a part of the face on one side, or may extend somewhat across the median line.

But little is known of causes underlying the condition. Of the twenty-three cases collected by Sabrazès and Cabannes eighteen were congenital. In Schick's case the hypertrophy commenced in the second year with no known cause. In Berger's case there was an obstinate antecedent neuralgia of the fifth nerve. Montgomery's patient had brain fever when two years old. There was no neuralgia. When nine years of age the patient had an osteomyelitis of the left maxilla. About one year later hypertrophy first appeared in the gums of the left side. In Dana's case the patient was also affected with gigantism. It is probable that several distinct conditions have been described under the term of hemifacial hypertrophy. Among the theories advanced as to the etiology of the acquired cases may be mentioned irritation of the fifth nerve through its roots or the Gasserian ganglion, and chronic hyperæmia of vascular origin.

The enlargement may be first noticed in the bones, particularly about the orbit, giving the eyeball the appearance of being depressed in its socket. The bony hypertrophy gradually extends until the entire side of the head is included. In other cases (*e.g.*, Montgomery's) the process may begin in the soft parts, and the gums, skin, sebaceous glands, hair, connective tissue, muscle, and the bones become later involved. The enlargement of the blood-vessels may cause a reddening of the skin. The flow of saliva may be considerably increased.

There are few conditions which could be confounded with hemifacial hypertrophy. It has been suggested that it might be mistaken for hemifacial atrophy of the other side of the face; but anything more than a cursory examination could not fail to disclose the differences.

We know of no cases in which the hypertrophied tissues have been replaced by normal ones; but after a progression covering a period of several years it is probable that the condition may become stationary.

Treatment thus far has proved unavailing, either in limiting the course of the disease or in reducing the hypertrophy. *T. Stuart Hart.*

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Montgomery: Medical News, July 15th, 1893.
Dana: Journal Nervous and Mental Disease, November, 1893.
Sabrazès and Cabannes: Nouvelle Iconographie de la Salpêtrière, 1898, p. 343.

FŒTUS, DEVELOPMENT OF.—Our knowledge of the development of the fœtus was in an exceedingly fragmentary condition until Wilhelm His, the distinguished German anatomist, published twenty years ago his noteworthy "Anatomie menschlicher Embryonen." This was the first, and is to-day the most important work on human embryology. Previously there were isolated descriptions here and there of embryos of the first two months of pregnancy. Uncertainty as to the normal appearance often leads to the description of abnormal for normal ones, and the great difficulty in obtaining embryos of the first two months of pregnancy renders progress comparatively slow. The main sources of such material are from post-mortem examinations, operations, and abortions; so the human embryologist is thus dependent upon the courtesy of physicians and surgeons for his material.

Age.—In regard to the ages of embryos of the first two weeks much uncertainty exists. Length is not entirely reliable, owing to distortions and variability in size. In attempting to determine age from the last day of the last menstrual period as the date of conception, there is often the difficulty of inexact history. The following table indicates in a fairly accurate way the length and ages of embryos:

Age.	Length.	Age.	Length.
Two weeks	2 mm.	Three months	50 mm.
Three weeks	5 "	Four months	100 "
Four weeks	8 "	Five months	200 "
Five weeks	11 12 "	Six months	300 "
Six weeks	16 "	Seven months	370 "
Seven weeks	20 "	Eighth months	425 "
Eight weeks	25 "	Nine months	500 "

According to Mall their ages in days corresponds to the formula $\sqrt{100 \times (\text{length in millimetres})}$ for all embryos from 1 to 100 mm. long. Multiply the length of the embryo from vertex to the breech in millimetres by one hundred, and extract the square root, and the result will be its age in days. In embryos from 100 to 220 mm. long from vertex to breech their length in millimetres equals their age in days. Fig. 5140 indicates the relative sizes during the first eight weeks.

There are but few good collections of embryos in the world; the one at Leipsic and the one at Baltimore are the most important.

In development it is convenient to distinguish the three stages suggested by His. The stage of the ovum embraces the first two weeks; the embryonal stage from the third to the fifth week, during which time the characteristic embryonal features and the principal organs are established; lastly the fœtal stage, during which time the embryonal features change to those of the fœtus and full-term child.

The Ovum Stage.—There are no observations on normal ova of the first nine or ten days. It is evident

from the material of the latter part of the stage of the ovum that there is an early and precocious development of the chorion and villi.

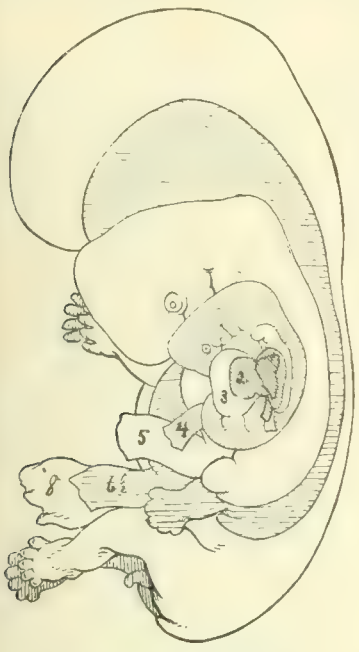

FIG. 5140. — Six Human Embryos taken from His' Standard Chart. Enlarged three times. The figures in the cut indicate the ages of the embryo in weeks. 2 is His' embryo S R.; 3, embryo Lr.; 4, embryo A.; 5, embryo C; 6½, embryo XCI.; 8, embryo Wt. (After Mall.)

The youngest known normal ovum was described by Peters in 1899. It is ten to eleven days old and consists of a vesicle 3 × 1.5 × 1.5 mm. in size. A section through the entire ovum is seen in Fig. 5141. The vesicle is formed by the chorionic membrane, consisting of an outer layer of epithelial cells covered by numerous villi which are in contact with the uterine wall of the mother, and an inner layer of mesenchyme. Attached to this inner layer at one side is the small embryo, but .19 mm. in length. It is apparently simple in structure, consisting of an epithelial plate facing the small amniotic cavity lined by flat epithelial cells, which are continuous with the epithelial cells of the plate. On the other side of the plate is a layer of mesenchyme, and projecting from this is the yolk sac lined by entodermal cells. The epithelial plate of the embryo, as well as the epithelium of the amnion, was probably at an earlier stage continuous with the epithelium of the chorion and the embryo, subsequently cut off after its sinking down or projecting into the vesicular cavity. One stage of such a process has been found in the monkey by Selenka. The projecting embryo is surrounded by mesenchyme continuous with that lining the chorion, as well as with that between the yolk sac and epithelial plate.

Already, then, in the youngest known ovum the so-called three primary germ layers are present. From these at a later period various structures arise. From the epithelial layer develop the epidermis of the skin and its appendages, such as hairs, nails, sweat glands, etc., the central nervous system, and portions of the eye and ear, mouth and nose. From the middle or mesenchymal layer develop the skeletal, muscular, circulatory, and urogenital systems; and lastly from the inner or entodermal layer, which is here represented by the lining of the yolk sac, develop the alimentary tract (pharynx, œsophagus, stomach, and intestines), the trachea and lungs, liver and pancreas, and bladder.

The next important human ovum was described by Spee in 1896. It measures 7 × 5.5 mm. and the embryo within is 0.37 mm. in length. Its age is about eleven days. The chorion is covered with villi and lined with mesenchyme (see Fig. 5142). The embryo is attached at one side by a broad pedicle, the so-called belly stalk. The amniotic sac is small and is continuous with the epithelial plate of the embryo, as in the preceding ovum. The primitive streak is represented in this embryo by a slight groove along the centre of the epithelial plate. Mesenchyme separates the epithelial plate from the large

FIG. 5141.—Peters' Early Ovum. (Enlarged about 35 diameters.) *U.E.*, Uterine epithelium; *Bl.L.*, lakes of blood; *Caps.*, decidua reflexa; *G.P.* "Gewebspilz"; *Dr.*, uterine glands: *U.Z.*, decidua vera; *Tr.*, trophoblasts; *C.*, capillaries; *K.A.*, beginning embryo; *Bl.G.*, large blood-vessels; *a–b*, point of entrance of ovum.

yolk sac, and a small diverticulum of the sac projects into the mesenchymal pedicle, constituting the first trace of the allantois. We thus see that the embryo in this ovum, although about twice as long as the Peters embryo, shows very little advance in structural differentiation. Both are in the primitive streak stage.

FIG. 5142.—Ovum Measuring 6 × 4.5 mm. Enlarged about 10 diameters. The left half of the chorion has been removed to show the embryo. *a*, Amniotic cavity; *b*, belly stalk; *c*, chorion; *e*, embryonic disc; *v*, chorionic villus; *y*, yolk-sac. (von Spee.)

Spee also described an ovum 10 × 8.5 × 6.5 mm. containing an embryo 1.54 mm. in length and about eleven and one-half days old. The chorion is covered by large branching villi, lined by mesenchyme, and attached at one side by a short pedicle is the embryo (see Fig. 5143). The primitive streak still persists, and near its anterior end the neurenteric canal has formed, thus connecting the amniotic cavity with the yolk sac. All traces of it are soon lost. More anteriorly still are traces of two longitudinal ridges, short distances on either side of the median line. These are the so-called medullary folds and are the first traces of a differentiation for the central nervous system. The allantois as in the preceding embryo projects from the yolk sac into the pedicle or belly stalk.

Between this stage and the next one we shall consider, the embryonic plate changes from a flat discoidal structure to a somewhat cylindrical body by a bending ventrally of its lateral edges, to which the amnion is attached, thus gradually constricting the broad attachment of the yolk sac. At the same time the head and tail ends begin to project more and more, and the yolk sac is thus also constricted in an anterior posterior direction. Connecting pockets of the yolk sac remain at both the head and tail ends of the embryo to form the beginnings of the digestive tract. During this time the medullary folds have lengthened and grown toward each other, so as to meet in the mid-dorsal line, thereby enclosing a central canal, the beginning of the central canal of the spinal cord and the ventricles of the brain. In the next oldest ovum we are to consider, which was described by Eternod, there was an embryo 2.11 mm. in length. The medullary folds have not only met, but are fused for a considerable portion of their length to form the neural tube (see Fig. 5144). The head of the embryo now projects some distance beyond the constricted yolk sac, and on the ventral side of this head fold is a slight invagination of the ectoderm for the mouth. Between the mouth invagination and the attachment of the yolk sac the heart is in the process of development from two lateral tubes, which soon fuse together to form the simple tubular heart. The blood-vessels which have developed in the extra embryonic area and those that have developed in the body of the embryo have now become connected with the heart, and at its head end arises the ventral aorta dividing immediately into three pairs of branchial arches, which pass around the primitive foregut to unite beneath the medullary plate into the dorsal aorta.

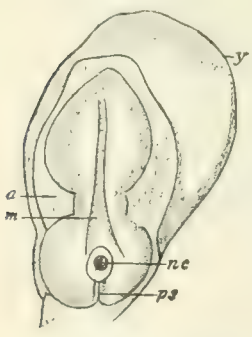

FIG. 5143.—Embryo 1.54 mm. in Length, from the Dorsal Surface. (Enlarged about 20 diameters.) *a*, Amnion; *m*, medullary groove; *nc*, neurenteric canal; *ps*, primitive streak; *y*, yolk sac. (von Spee.)

From the dorsal aorta are given off the omphalo-mesenteric and the umbilical arteries. The first veins to develop are those which accompany the first formed arteries, namely, the omphalo-mesentericus, connected with the yolk sac, and the umbilicals, connected with the allantois. Soon after these are formed the veins within the body of the embryo develop, the first ones being the anterior cardinals, or internal jugulars and the inferior cardinals, the latter draining the blood from the caudal portion of the body. An anterior and a posterior cardinal of each side unite to form the ductus Cuvieri. The two ducts, one on either side, pass transversely toward the median line and open into the sides of the sinus venosus. The omphalo-mesenteric veins coming from the yolk sac and the umbilicals from the allantois join the sinus venosus at a slightly earlier date than do the Cuvierian ducts. At a later stage we shall see how this primitive arrangement is modified to form the adult condition. The yolk sac in this embryo is somewhat constricted along its attachment, leaving pockets of entoderm connected with it that lie in the head and tail ends of the embryo. They form the primitive foregut and hindgut. At either side of the neural tube the mesenchyme has become differentiated into eight prim-

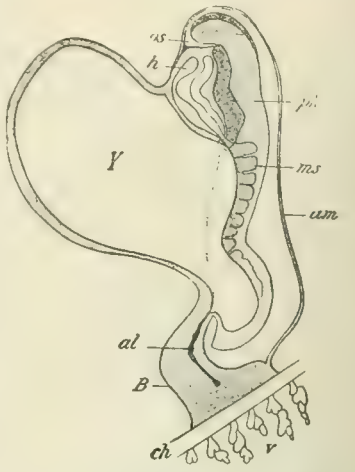

FIG. 5144.—Reconstruction of Embryo 2.11 mm. Long. (Enlarged about 25 diameters.) *al*, Allantois; *am*, amnion; *B*, belly stalk; *ch*, chorion; *h*, heart; *ms*, mesodermic somite; *os*, oral fossa; *ph*, pharynx; *v*, chorionic villi; *Y*, yolk-sac. (After Eternod.)

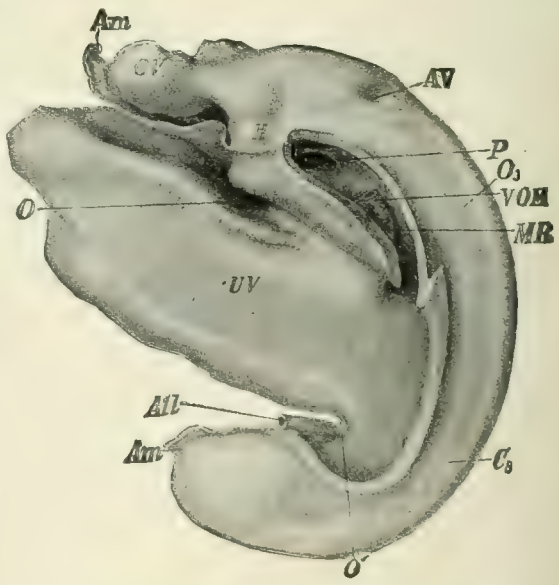

FIG. 5145.—Profile Reconstruction of the Embryo, 2.11 mm. Long. No. XII. × 37 times. *Am*, Amnion; *OV*, optic vesicle; *AV*, auditory vesicle; *UV*, umbilical vesicle; *H*, heart; *VOM*, omphalo-mesenteric vein; *MR*, septum transversum; O_3, third occipital myotome; C_8, eighth cervical myotome. (After Mall.)

itive segments or myotomes, from which later much of the muscular system becomes differentiated.

A slightly older embryo, of about the same length, described by Mall, consists of an ovum measuring 18 × 8 × 8 mm., and containing an embryo 2.1 mm. in length. The age is about two weeks (see Fig. 5145).

Many important changes have taken place. The embryo is connected to the chorion by a thinner stalk of mesenchyme containing the blood-vessels that carry on the circulation between the embryo and chorion, the latter being in close contact with the uterine wall, and thus affording opportunity for nourishment and oxygen to pass from the mother through the thin walls of the villi, to supply the rapidly growing embryo with the essentials for growth and life. The embryo itself has greatly increased in length, and is curved into a semicircular form. The medullary plate is converted into a tube and the groove into its canal. At the anterior end of this tube are enlargements marking the beginnings of the brain. The remainder of the tube forms the spinal cord. The yolk sac, which is covered by blood-vessels that communicate with those of the embryo, is more constricted and the fore- and hindguts are longer than in the preceding stage. From the foregut arises the pharynx with two gill pockets and a thyroid pocket. The neurenteric canal connects the hindgut with the central canal of the central nervous system. So while from the yolk sac are differentiating the two ends of the alimentary tract, the main portion is still embodied in the large sac. Near the origin of the foregut is a slight projection of the yolk sac for the beginning of the liver. In the anterior wall of the yolk sac, posteriorly to the mouth and beneath the pharynx, is the tubular heart. There are now fourteen pairs of mesenchymal segments or myotomes—three in the head, eight in the neck, and three in the thoracic region. The amnion at this period forms a small sac about the dorsal surface of the embryo.

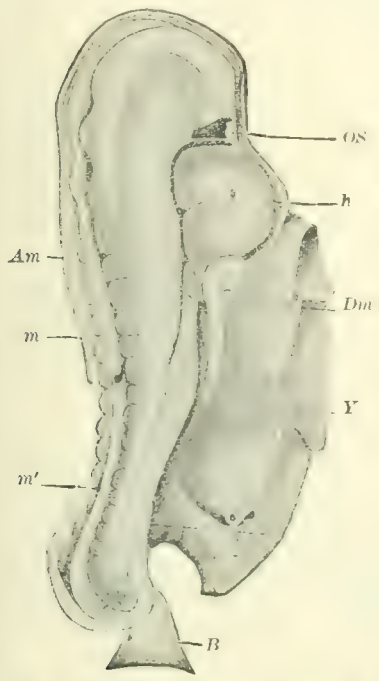

FIG. 5146. Embryo 2.5 mm. Long. (Enlarged about 33 diameters.) *Am*, Amnion; *B*, belly stalk; *h*, heart; *m*, closed and *m'*, still open portions of the medullary groove; *Om*, omphalo-mesenteric vein; *OS*, oral fossa; Y, yolk sac. (Kollmann.)

In an embryo described by Kollmann (Fig. 5146), and measuring 2.5 mm. in length, the edges of the medullary folds have come in contact throughout their entire length except for a short distance anteriorly, and thirteen pairs of mesodermic somites or myotomes are visible. The constriction of the yolk sac is even more pronounced than in the preceding embryo, and the hind end of the body has become defined, the belly stalk no longer seeming to be a posterior continuation of the body, but arises from the ventral surface. The oral fossa is more marked.

The general shape of this embryo is quite different from that of the preceding one, the embryo being nearly straight; and it has probably been distorted, as has also the His embryo (Fig. 5147), as the normal curve of the medullary tube at this period is probably somewhat semicircular, as seen in Figs. 5145 and 5149. This so-called dorsal flexure, which is often pictured in text-books as a normal condition at this stage, I have been able to produce in pig embryos of a corresponding stage by rough handling while removing them from the uterus. Others from the same uterus, which were more carefully handled, do not show such a dorsal flexure, and we naturally conclude that similar treatment has produced a similar effect in the human embryo.

The His embryo Lg, 2.15 mm. long, contained in an ovum 15 × 12.5 mm., is the next important one to consider. Its age is about fourteen days. (Fig. 5147.) The forebrain has a marked ventral bend. Between the forebrain and the heart is now a well-marked invagination of the skin to form the mouth cavity. It is not as yet connected with the pharynx. Projecting from the forebrain are the optic vesicles, and farther back are invaginations of the ectoderm for the internal ear. Two gill clefts and three branchial arches are present, and branches of the aorta pass through the latter. The heart consists of a much bent tube.

The branchial arches and clefts are of great morphological importance, since they determine to a large extent the arrangement of the various organs of the head region. In the human embryo four clefts and five branchial arches appear on each side. The last arch is very indistinct.

We thus see that during the first two weeks, which constitute the ovum stage, there has developed from the simple one-celled ovum or egg an embryo with its membranes, the amnion and chorion, the latter having over its entire surface numerous long branching villi, and in the embryo are already present the beginnings of the central nervous system, the alimentary tract, the circulatory system, the muscular and skeletal systems, the latter being represented by the chorda dorsalis, which has differentiated from the dorsal wall of the entodermal sac and canal. The primitive urogenital system has also begun to appear. The yolk sac remains throughout this stage the dominant feature of the embryo.

The Embryonal Stage.—During the third week the embryo grows rapidly in size and attains a length of about

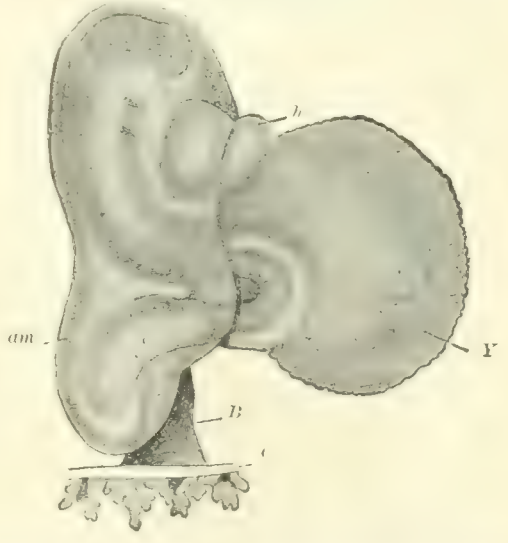

FIG. 5147.—Embryo Lg., 2.15 mm. Long. (Enlarged about 30 diameters.) *am*, Amnion; *B*, belly stalk; *C*, chorion; *h*, heart; Y, yolk sac. (His.)

4 mm. The brain increases in size and shows the three primary divisions. The optic and otic vesicles become more prominent. Two more gill clefts and three more gill arches appear caudal to the ones already formed. The attached area of the yolk sac has diminished. The

mouth cavity communicates with the pharynx. By the twenty-first day the limb buds appear (see Fig. 5148). Internally the heart is enlarged and takes the form of an S-shaped tube. From the aorta now arise five pairs of

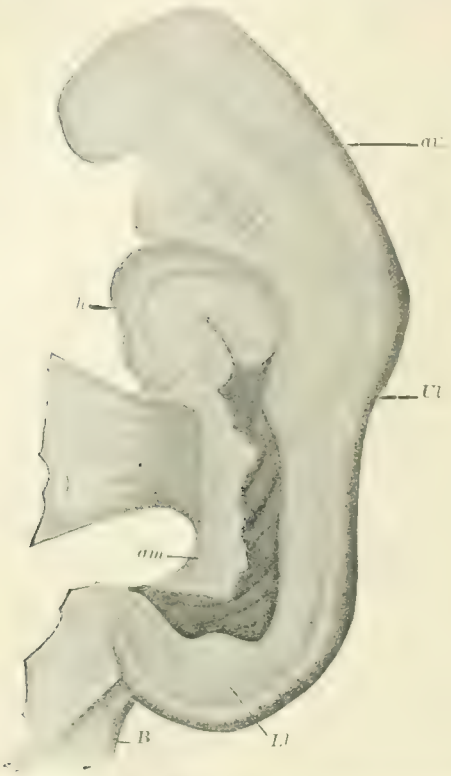

FIG. 5148. Embryo Lr., 4.2 mm. Long. (Enlarged about 23 diameters.) *am*, Amnion; *au*, auditory capsule; *B*, belly stalk; *h*, heart; *Ll*, lower and *Ul*, upper limb; Y, yolk-sac. (His.)

arteries which pass through the five pairs of gill arches, joining on the dorsal side of the pharynx into the common dorsal aorta.

By the narrowing of the attachment of the yolk sac more of the primitive gut has been folded off, so that now the foregut, midgut, and hindgut are to be distinguished. In the foregut can already be made out the pharynx with its diverticula, the œsophagus, and the stomach. Of the pharyngeal diverticula there are four pairs of gill pockets corresponding to the gill clefts on the external surface and separated from the gill clefts by a thin membrane. The diverticulum for the respiratory tract has begun to bud from the œsophagus. The first indication of the lungs and trachea is found in embryos of about 3.2 mm. in length in the form of a groove, the pulmonary groove, along most of the ventral surface of the œsophagus. During the embryonal stage this groove deepens especially toward the stomach, where it ends in a a rounded projection, which lengthens and gives off branches. These, by repeated branching, give rise to the various-sized bronchi and the epithelial portion of the lungs. The pulmonary groove gradually becomes constricted off from the œsophagus to form the trachea. At the upper end, however, it remains open into the pharynx, in the region of the fourth branchial diverticulum, to form the glottis. The midgut gives rise to the small intestine and to a portion of the large intestine. From it have arisen diverticula which give rise to the liver and pancreas. The hindgut gives rise to the rest of the large intestine and to the rectum.

The primitive urogenital system has appeared as two longitudinal ridges projecting into the cœlom along its dorsal wall, one at either side of the median line in the posterior half of the embryo. This ridge contains the Wolffian duct, the pronephros with its two tubules and rudimentary glomeruli. The Wolffian duct, which is the first to appear, develops from the mesenchyme, and extends from the heart region to the cloaca. Soon after the non-functional pronephros is formed, the mesonephros begins to develop and its tubules join the Wolffian duct. The mesonephros is a much more important structure than the pronephros, and we shall consider it again later. The beginning of the Müllerian duct is also present at this stage.

During the fourth week growth is relatively more active than at any other time, except during the very early stages of the first week or ten days. The embryo about doubles in length, and attains a length by the end of this week of about 6 or 7 mm. During the first part of the week the embryo becomes very much flexed, so much so that the head and tail nearly touch. The brain vesicles are better developed, as are also the gill clefts and arches, the eyes, ears, and nasal pits. The heart, which is much enlarged, lies in the cervical region, near the mouth, and produces with the liver, which is now of considerable size, a large ventral bulge. The simple tubular heart with its single cavity is rapidly changing into a complicated four-chambered structure with imperfect partitions. By the end of the fourth week (see Fig. 5149) the anterior enlarged portion of the head has become bent at right angles to the main axis of the body. From the first gill arch a maxillary process is developing which will ultimately form a portion of the upper jaw. From the main portion of the arch will form the lower jaw. The limb buds have increased in size. The arm bud projects from the cervical region and the leg bud from the lumbar region. The yolk sac is very small and the amniotic sac is much enlarged. During the early part of the fourth week the intestinal tube, composed of its several characteristic segments, lies in the sagittal plane attached to the dorsal wall of the body cavity by the straight primitive mesentery. Toward the last of the week rapid growth takes place, the intestine lengthens, and becomes coiled and twisted.

The nerves have begun to grow from the medullary tube or central nervous system into the mesenchyme. Plexuses are forming, but the nerves are not attached to their end-organs. There are now thirty-eight primitive segments or myotomes which have been formed from the mesenchyme lateral to the spinal axis. Muscle fibres are beginning to differentiate from the cells of these segments. Their ventral ends have begun to grow into the primitive abdominal wall formed by the growing around of the amnion. Condensed mesenchyme marks portions of the vertebral column. In the arm bud the mesenchyme is beginning to differentiate to form the skeletal core of condensed mesenchyme. The Wolffian ridge has increased in size and the Müllerian duct is now formed and runs parallel with the Wolffian duct. A diverticulum from the lower end of the Wolffian duct near the cloaca indicates the beginning of the permanent kidney and its duct, the ureter. On the Wolffian ridges are also seen the first traces of the sexual glands, but they are indifferent in type, and not until the fifth week can sex be determined by microscopical examination.

By the middle of the fifth week the embryo is 9 mm. in length. The amniotic sac is now so much enlarged that it is everywhere in contact with the chorion. A true umbilical cord of some length has developed by the enclosure of the entire belly stalk and yolk stalk within a tubular prolongation of the embryonic ectoderm and somatic mesoderm of the embryo. The embryonic ectoderm at the end of the cord is continuous with the extra embryonic ectoderm of the amnion, and the somatic mesoderm with that of the amnion, which is in contact with that of the chorion. So, strictly speaking, the umbilical cord is a portion of the embryo, the amnion having been carried farther and farther from the umbilicus by extension of the embryonic ectoderm. The head is as large as the rest of the body, and bent at right angles to it. Its

large size is due to the rapid growth of the brain. The three primary divisions of the brain are more marked and bent upon each other. From the forebrain the cerebral hemispheres have begun to grow. The spinal cord forms a thick walled tube of nervous tissue. The various cranial and spinal nerves now extend some distance into the body and the motor nerves of the head and shoulder reach the premuscle masses. The rami communicantes are already present at this stage and connect with the sympathetic cord. The latter forms a continuous column of cells in front of the vertebræ, and has not as yet separated into ganglia. The sympathetic nerve cells have reached this position by migration from the ganglia of the dorsal roots.

At about this time the suprarenals commence their development and are found, at the beginning of the third month, occupying their characteristic position as a cap fitted over the head of the kidney. They rapidly acquire a very large size and at birth have their permanent volume. There is no developmental relation between the suprarenals and the kidney. The suprarenals are probably derived partially from the mesonephros and partially from the sympathetic nervous system, the latter giving rise to the medullary portion and the former to the cortical portion.

The gill clefts and arches are undergoing marked changes. From the first arch the upper and lower jaws

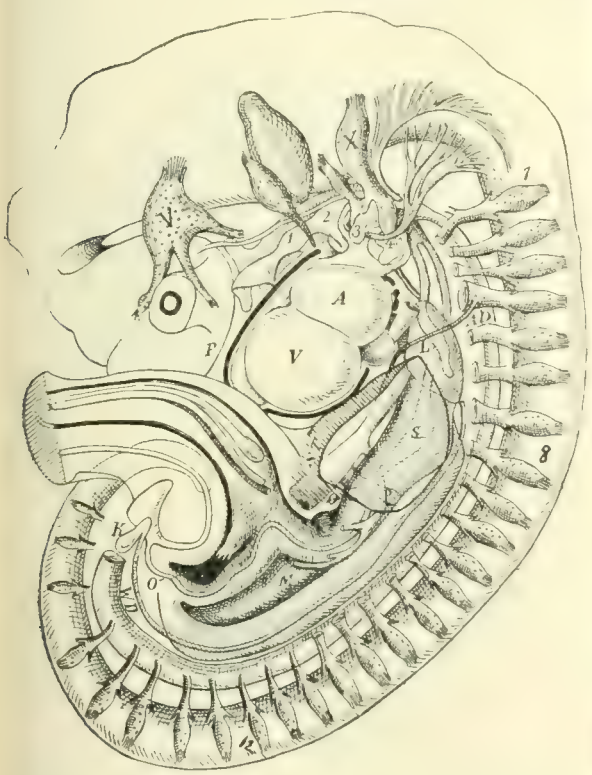

Fig. 5149.—Reconstruction of Embryo No. II., Johns Hopkins University Collection. (Enlarged 17 times.) *V* and *X*, Fifth and tenth cranial nerves; *1*, *2*, *5*, and *8*, cast of the branchial pockets; *1* and *8*, first and eighth cervical nerves, from the fourth the phrenic arises; *12*, twelfth dorsal nerve; *A*, auricle; *V*, ventricle; *L*, lung; *S*, stomach; *P*, pancreas; *W D*, Wolffian body; *K*, kidney; *M*, mesentery; *S T*, septum transversum; *O*, openings which communicate with the peritoneal cavity of the opposite side. The black line around the heart marks the pericardial cavity. (After Mall.)

are developing. From the first cleft the external auditory canal and ear drum are forming, and from the pharyngeal portion of the cleft the Eustachian tube and middle ear. The malleus and incus of the ear arise from the dorsal portion of the cartilage of the first gill arch, and from its ventral portion Meckel's cartilage. From the second arch are forming the stapes, styloid process, and the hyoid apparatus, to which later the tongue muscles become attached. The remaining arches and clefts are beginning to disappear by sinking into the depth of the neck, re-

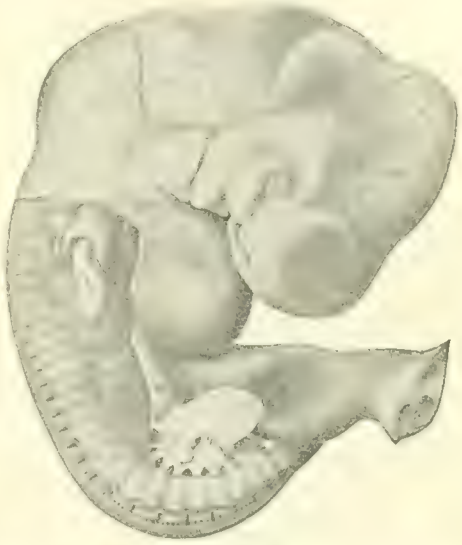

Fig. 5150.—Lateral View of a Human Embryo 9 mm. in Length and About Four and One-half Weeks Old. No. CLXIII. Johns Hopkins University Collection. (Enlarged about 8 diameters.) The areas from which the skin has been removed are drawn from reconstructions, the remaining portions from excellent photographs. The myotomes are growing into the body wall. Portions of the premuscle masses of the arm are seen and also the preskeletal tissue of the arm and leg with the beginnings of the lumbar sacral plexuses. (After Bardeen and Lewis.)

maining connected with the surface, however, by a deep sinus, the so-called cervical sinus. Occasionally one may persist to adult life as a sinus or cyst. The arm and leg are enlarged and show two segments (see Fig. 5150). The skeletal system consists of a condensed mesenchymal tissue and precartilage. The premuscle masses of the head and arm are differentiating from the mesenchyme. Those of the trunk arising from the myotomes contain muscle fibres and are more advanced, while those of the limbs appear to develop *in situ* about the preskeletal mesenchyme, and show no fibrillation. The heart still lies close to the mouth in the neck region. It is much changed in shape and is imperfectly four-chambered. The truncus arteriosus is undergoing division into two tubes by the formation of the aortic septum.

The modification of the primary arterial system is progressing rapidly. The main portions of the first two arches have disappeared, giving rise with the third arch to the common carotids and their branches. From the last arch the pulmonary arteries are developing, and from the fourth, which seems to be a combination of the fourth and fifth, develop the large aortic arch on the left side and innominate and subclavian on the right side. The latter, however, still retains its connection with the dorsal aorta, giving a condition found in reptiles. The important connection of the last arch on the left side with the aorta remains of large size, and that portion of it between the pulmonary artery and the aorta forms the ductus arteriosus, a very important fœtal structure, as it enables the venous blood from the right side of the heart to pass into the aorta without going through the lungs. The growth of the liver has also been an important factor in bringing about modifications in the venous system. With the diminution of the umbilical vesicle the extra embryonic portion of the omphalo-mesenterics disappears, but the embryonic portions of the two veins form the portal

system. Of the two umbilical veins, the left persists entire, to form the single umbilical vein of the embryo and cord. The right umbilical vein degenerates into an unimportant vein. The presence of the liver has also modified the proximal ends of the umbilical veins. The left one becomes divided into a capillary net, which

FIG. 5151. Lateral View of a Human Embryo 11 mm. in Length and About Five Weeks Old. No. CIX., Johns Hopkins University Collection. (Enlarged about 7 diameters.) The dissected area was drawn from a reconstruction. (After Bardeen and Lewis.)

again collects into a short vein that opens into the sinus venosus. The development of the ductus venosus soon forms a channel for most of the blood carried by the umbilical vein. The proximal portion of the inferior vena cava is developed as a new structure. The distal end of this unites with the right inferior cardinal in the region where the renal arteries arise; and the caudal continuation of the cardinal from this point of union becomes the inferior portion of the vena cava. The remaining portions of the two cardinals form the azygos veins. A cross anastomosis develops from the left jugular to the right jugular, and from the common stem thus formed develops the superior vena cava. The proximal portion of the ductus Cuvieri on the left side then loses its connection with the jugular and becomes the coronary sinus of the heart.

By the time the embryo is five weeks old it has attained a length of 11 mm. (see Fig. 5151). The head is still very large and bent at right angles to the main axis of the body. The maxillary and nasal processes, which fuse at a later stage to form the upper jaw, are now more marked and approaching each other. The external nares are nearing the middle line. The external ear is represented by several small protuberances about the first cleft. The general body musculature is well advanced and has its nerve supply. The ribs and the muscles of the thorax and abdomen have grown some distance into the thin membrane, membrana reuniens, which in early stages constitutes the ventral body wall. The limbs are much enlarged and contain a skeletal core of cartilage surrounded by the developing muscles. The arm keeps about two weeks in advance of the leg in its internal differentiation. The vertebral column and ribs are formed partially in cartilage. The fourth pair of the aortic arches still persists entire and the others are modified in various ways to form the larger arteries in this region. The liver has been increasing rapidly in size, and in this embryo as in the preceding stage forms with the heart most of the large projecting abdomen and thorax. The allantois forms a long narrow tube extending from the hindgut into the umbilical cord as far as the chorion. At a later stage the umbilical portion becomes obliterated, while the portion near the hindgut enlarges into the bladder.

During the fifth week the œsophagus elongates and the stomach acquires its characteristic form, as well as an obliquely transverse position, its former left side becoming directed anteriorly and upward, and its former right side looking backward and downward. This explains the distribution of the left vagus nerve to the front of the stomach and the right to the back; for, before this twisting of the stomach began, these nerves had already reached the stomach. The connection of the yolk stalk or vitelline duct with the intestinal canal rapidly becomes less marked, and by the end of this week only a small duct attaches the yolk sac to the intestine.

During the last part of the embryonal stage and the first part of the fœtal stage there are very important shiftings or migrations of various organs in the body. That of the heart and diaphragm from the cervical region into the thoracic region is of especial interest, as other structures are dragged along with them. The large blood-vessels are pulled downward, and such nerves as the recurrent laryngeals indicate this process. Originally they passed directly from the vagus to the larynx just posterior to the fifth aortic arch, and by the migration of the heart and large blood-vessels they are brought into the position seen in the adult. The diaphragm in its descent obtains muscle tissue and its nerve in the cervical region,

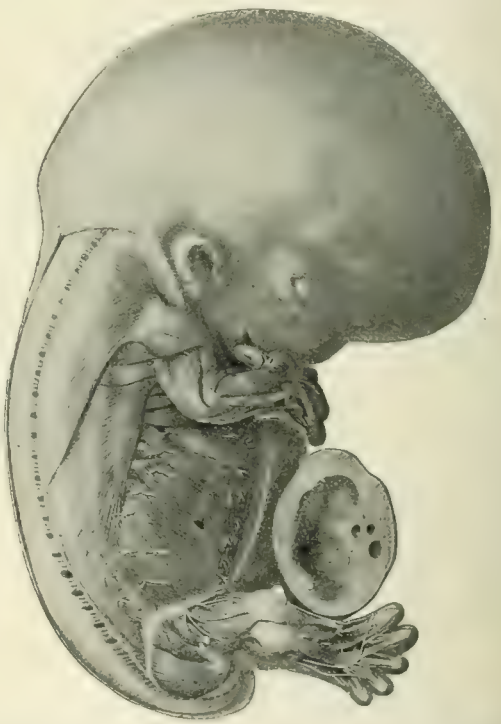

FIG. 5152.—Drawing from a Reconstruction of a Human Embryo 20 mm. in Length and About Seven Weeks Old. No. XXII., Johns Hopkins University Collection. (Enlarged about 5 diameters.) The muscular systems of the limbs and body wall are seen to be well developed. (After Bardeen and Lewis.)

and both are then carried down to the lower part of the thorax. The limbs also exhibit a migration, the arm from the cervical to the thoracic region giving the caudal inclination to the brachial plexus, which originally went straight out into the arm without this caudal inclination. The leg likewise migrates. Many individual muscles also take part in this shifting and migrating, such as the trapezius from the upper cervical region and the

latissimus dorsi from the lower cervical. The path of the nerve from its exit at the intervertebral foramen to its point of entrance into the muscle indicates the path the migrating muscle has taken, while the branching within the muscle probably indicates the direction in which the muscle has increased in size.

During the embryonal stage the yolk sac has diminished to an organ of relatively small size and importance, while the central nervous system, with its greatly enlarged anterior end, the brain, giving to the head its great prominence, becomes the predominating feature of the embyo. The head throughout most of this stage is about equal in bulk to the rest of the body of the embryo.

Fœtal Stage.—In an embyro seven weeks old and 20 mm. long the early fœtal features are fairly well marked. The head is nearly erect. The fusion of the maxillary and nasal processes is proceeding rapidly to form the upper jaw, and the nasal pits have approached nearer to the median line. Failure of fusion between these processes gives rise to the various forms of cleft palate and harelip. The arms and legs are much elongated, and show the three segments seen in adults. Fingers and toes are also to be distinguished. Practically every muscle of the body can now be recognized, and has also its nerve supply (see Fig. 5152). Most of the skeletal elements are present in cartilage. Portions of the skull, however, are never so represented, but ossification takes place directly from the condensed mesenchyme. The ribs have extended nearly to the mid-ventral line. The thoracic and abdominal muscles have likewise pushed farther out into the ventral wall of the body.

By the end of the second month the permanent kidney is fairly well formed and the Wolffian body, which so far in the life of the embryo has performed the function of an excretory organ, begins to lose its importance. All but the middle portion, which later forms the sexual gland, atrophies. Its duct in the male forms the vas deferens, in the female degenerates, while in the female the Müllerian ducts form the Fallopian tubes and uterus, and in the male degenerate. Thus by the end of the second month most of the organs which are found in the adult are formed. The main processes which now take place until birth are the growth and shifting about of these organs.

The *third month* establishes the human form, although the head still unduly predominates. The limbs have acquired their definite shape, and the imperfect nails are present on both fingers and toes. The external organs of generation become definitely differentiated, although they make their appearance several weeks earlier.

In the female the genital tubercle remains much less developed to form the clitoris. The genital furrow remains open to form the vestibule and the genital swellings the labia majora. The prepuce and labia minora developing from the genital folds, lie at either side of the genital sinus. The genital swellings in the male when they develop into the scrotum have layers identical with those of the abdominal wall, as seen in the following scheme:

Abdominal Walls.	*Scrotum.*
Integument.	Integument.
Superficial fascia.	Dartos.
External oblique muscle.	Intercolumnar fascia.
Internal oblique muscle.	Cremasteric.
Transversalis muscle.	Infundibuliform fascia.
Peritoneum.	Tunica vaginalis.

The tunica vaginalis lines the sac, communicating above with the peritoneal cavity; and into this sac later the testicle descends. The anterior end of the ureter now reaches the neighborhood of the suprarenal where it ends in the kidney, which consists of about eighteen lobes, one for each group of tubules connected with the ureter. This lobulation persists until after birth. The suprarenals now fit caplike over the anterior end of the kidney. At the end of the month the fœtus weighs about 120 gm. (3¼ ounces), and measures about 5 cm. (2 inches) in length.

During the *fourth month* hairs devoid of pigment appear on the scalp and other parts of the body, which is now covered with firmer skin of a rosy hue. The eyelids, nostrils, and lips are closed. The anus opens, and the coils of intestine, which before extended into the umbilical cord, now lie entirely within the abdominal cavity. The point of emergence of the umbilical cord lies low down close to the pubes. The head forms about one-fourth of the entire body. The bones of the skull while ossifying are still widely separated. The sexual distinctions of the external genital organs are well defined. By the end of this month the fœtus weighs about 230 gm. (7½ ounces), and measures about 10 cm. (4½ inches) in length.

During the *fifth month* the lower extremities become longer than the arms, nails are well formed, and hairs are more plentiful, but devoid of color. The fœtal movements are distinctly felt by the mother. The sudoriparous glands arise during this month as solid cylindrical outgrowths from the primary ridges of the epidermis into the dermis. Later they become coiled and a lumen appears. The heart and liver share with the head in the undue preponderance which these parts present. At the end of this month the fœtus measures 20 cm. (8 inches) in length, and weighs about 500 gm. (1 pound).

During the *sixth month* the surface presents many wrinkles and is of a dirty reddish hue; the sebaceous coating, the vernix caseosa, begins to appear. This whitish substance is composed of shed surface epithelium, mingled with the secretions of the sebaceous glands; its primary function seems to be the protection of the integument from maceration by the amniotic fluid. The eyebrows and eyelashes begin to grow. . The length of the fœtus by the end of this month is about 30 cm. (12 inches), and its weight about 1,000 gm. (2 pounds).

The Seventh Month.—The formation of fat causes an appearance of greater plumpness, although the surface is still somewhat wrinkled. The hairs are longer, about 5 mm. in length. The eyelids are now permanently open. The liver is still relatively large; the testicles have descended as far as, or even into, the inguinal canals. Children born at the end of this month may live. The fœtus measures at the end of this period about 37 cm. long (15 inches), and weighs about 1,500 gm. (3 pounds).

The Eighth Month.—This and the ninth month complete the fœtal period. The chief changes are great increase in weight, as by the end of the eighth month the fœtus weighs from 2 to 2.5 kgm. (4 to 5 pounds) and measures about 42 cm. in length. The scalp is well supplied with hair, and the finger nails almost reach the finger tips. The lanugo or embryonal down begins to disappear. The subcutaneous fat has increased considerably, giving a more rounded form to the body.

The Ninth Month.—During this month there is a relatively large increase in weight, from 2 to 2.5 kgm. to about 3 or 3.5 kgm. (6 to 7 pounds), while the increase in length is only from about 42 to 50 cm. (20 inches). The skin is less highly colored and the lanugo has almost entirely disappeared. The testicles have descended into the scrotum; in the female the labia majora are in contact. Centres of ossification usually appear in the epiphysis at the lower end of the femur, and often in the upper epiphyses of the tibia and humerus.

Warren Harmon Lewis.

GIGANTISM, GENERAL.—The word giant is derived from the Middle English "geant," the equivalent of the French "géant," which may be traced back to the Greek γίγας.

Very early in the world's history we meet with references to huge beings of supernatural strength. Even before the flood, in the story of Noah, we are informed that "there were giants in the land in those days," and there are stray allusions to giants, Emmim and Anakim, in the accounts of the early Jewish conquests, in the sight of whom the people were "as grasshoppers," to use

the characteristic Eastern hyperbole. Later, we have the celebrated battle between David and Goliath of Gath, one of the few remaining descendants of these Anakim, whose height was six cubits and a span. The Greeks, also, had their giants in the man-eating Cyclopes and Lestrygones. The Titans, too, forty-five in number, whose children were the Gigantes, were of enormous size. They did not fear to encounter the gods, and were said to have heaped up mountains, to have "piled Ossa on Pelion," in order to scale the heavens. All nations, alike in their love of the marvellous and their sympathy with the weaker side, have their stories of unequal battles, recalling the struggle between the pygmies and the giants, waged between brave men and monsters of immense size and strength, in which the lesser power comes off the conqueror. An instance that will be familiar to all is the popular nursery tale of "Jack the Giant-killer," which used to delight us so much in our youth. As is usually the case, human credulity and the innate tendency to exaggeration have magnified many of these tales beyond the bounds of credibility. While it must be admitted that in former times there have been individuals and even races that far exceeded in strength and stature the ordinary run of mankind, the application of the rigid canons of modern scientific inquiry has resulted in the dethronement of the supernatural element and the reduction of the subject, though marvellous enough still, to more manageable proportions. Before passing on to discuss the nature of this curious anomaly of development that we call gigantism, we may with advantage pause for a moment to determine what constitutes giant growth.

This is not so easy as it seems. If any one asks himself the question, "Where does giant growth begin?" he will at once realize that his ideas are somewhat hazy and his language conventional. In popular parlance a giant may be said to be any individual who exceeds in a notable degree the average height of human beings. A person of six feet six or upward would probably be called gigantic. This is, of course, an exceedingly loose and by no means scientific definition. It fixes no limits, it takes no account of weight and strength; in short, it lacks precision. Larcher[1] defines a giant to be "A being who, free in other respects from all defect in the essential characteristics of the organization, excels notably in height other beings of the same race who have reached adult age." In such a case the structural harmony and the relationships between the different parts are manifestly normal, the sole deviation being the striking increase in height. It is scarcely necessary to point out that this definition portrays for us the ideal or perfect giant, a being rather more imaginary than real. No doubt there have been individuals of great size and strength, handsome, well proportioned, and well balanced in all their faculties, but these are the *rarœ* or rather the *rarissimæ aves*. As a matter of fact, the immense majority of giants present the unmistakable stigmata of defect or degeneration. The definition further ignores the fact that gigantism is a process, an anomalous one it is true, but still a process of growth which may and does manifest itself in embryonic life and childhood, as well as in the adult stage. Pierre Marie[2] recognizes two forms of gigantism: (1) *True gigantism*, consisting in a simple exaggeration of the normal process of growth; and (2) *symptomatic gigantism*, a manifestation of pre-existing disease. Meige[3] would restrict the term gigantism to Marie's second class on the ground that the members of the first group are in all respects normal persons, differing in no way, save in height, from other individuals of the same species. This, while no doubt contributing to precision of language and lessening the possibility of confusion in description, is in my opinion too extreme a position to take, for who will maintain that an exaggeration of a normal process of growth is not a pathological manifestation? We ought not, therefore, rashly to conclude that true gigantism and symptomatic gigantism are necessarily or essentially different processes, or that the former should be left out of our consideration of the general subject of gigantism. We shall be helped considerably toward a proper conception of what constitutes giant growth if we consider briefly what may be called the "law of deviation" enunciated by Thoma.

Thoma[4] states, on the basis of an extended series of observations, that in adults the normal length of the body averages approximately 169 cm. in the male and 163 cm. in the female: the normal average body weight is 60 kgm. and 56 kgm. respectively. Considerable variations on one or other side of this norm occur. In one-half the total number of individuals the amount of deviation is anywhere from 0.0 to 3.8 cm. for height, and from 0.0 to 5 kgm. for weight. In accordance with observations he has made, Thoma finds that the fifth multiple of the figures representing the amount of normal deviation, namely, 19 cm. and 25 kgm., is exceeded only once in a thousand individuals. According to this an adult male would be regarded as a giant if his height exceeded 169 plus 19 or 188 cm., or if his weight were more than 60 plus 25 or 85 kgm. The normal limits, however, for the upper well-nourished classes are somewhat higher than the figures given, namely, 175 cm. and 66 kgm., so that the lower limit for giant growth would be more correctly placed at 175 plus 19 or 194 cm., and 66 plus 25, or 91 kgm. (6 feet 4½ inches, and 200 pounds 5½ ounces). In the case of new-born infants the normal average for length is 50 cm. and for weight 3.2 kgm. The amount of deviation is approximately 1.4 cm. and 0.28 kgm. respectively. Applying the same rule we may assume giant growth in children if they exceed 57 cm. in length and 4.6 kgm. in weight. For Thoma, then, a giant is literally a man in a thousand. We cannot, however, assume that because an individual exceeds these dimensions he is necessarily a giant. It should be noted that height and weight are not necessarily closely correlated. In true gigantism no doubt they would be, but in many cases we find that those gigantic in stature are not heavier than many normal persons. This is often to be explained on the score of some wasting disease which is present, or that the individuals in question have died or been observed before the consolidation of the body had been properly attained. Further, an excess in weight above the limit of 91 kgm. cannot in itself constitute gigantism, for this weight is frequently attained by those who would be regarded as normal individuals, and has also been attained in cases of diffuse lipomatosis, elephantiasis, and when large tumors are present. Gigantism is quite different from this. Properly understood, it implies not a mere increase in the bulk of any tissue or group of tissues, but rather an abnormal increase in the size of the body as a whole, due to some peculiar and inherent nutritive disturbance. The term *macrogenesy* would perhaps most correctly designate the condition.

Gigantism manifests itself in an excessive growth of the bones, more especially in the direction of length, but also to some extent in thickness. The long bones are most noticeably involved, but all the bones of the body may be to some degree affected. With this there is a corresponding increase in size of the nerves, vessels, and soft tissues generally. The most striking and constant feature in giants, however, is their great height. The deviation in weight is less apparent, is usually less and never more than the increase in height would warrant.

From a pathological standpoint gigantism belongs to the group of tissue hypertrophies, of which there are many less extreme manifestations than the complete giant. Local hypertrophies of undoubtedly developmental origin are not infrequently met with, particularly in the head and extremities. In the case of the head the bones of the cranium and face are usually involved, giving rise to an extensive and remarkable deformity (leontiasis ossea of Virchow), the exact nature of which is somewhat obscure but appears to be essentially a diffuse hyperostosis. The form found in childhood is especially common in the upper limbs, and may be unilateral or bilateral. Apart from these instances of local gigantism, which are characterized mainly by an abnormal increase in the bulk of the affected part, there are other condi-

tions, regarded by some as forms of gigantism, in which the excess is numerical, as, for example, polydactylism, accessory ribs and vertebræ, and supernumerary organs.

Gigantism, or macrogenesy, is comparatively rare as a congenital anomaly. Fuchs[5] in the extensive material of the Lying-in Hospital at Kiel found the average weight of the new-born child at full term to be from 3 to 3.5 kgm., figures which agree accurately with those given by Thoma. This limit was not often passed, and a body weight of 5 kgm. (11 pounds) was of the greatest rarity. In 3,600 births at the Dublin Rotunda only one child reached 5 kgm. Ahlfeld[6] in fifteen years' experience met with no case above 5.1 kgm. Spiegelberg and Wiener[7] observed two infants weighing 5.2 and 6 kgm. respectively. Baudelocque[8] in many years saw only one infant that reached 6.375 kgm. Fuchs (*loc. cit.*) has described in detail two infants that weighed 6.1 and 7.55 kgm. and measured 60 and 65 cm. respectively. The most extensive statistics are those of von Winckel,[9] who in 30,000 births found no child reaching 6 kgm.; in 17,000 cases at Munich only 5 were found weighing from 5 to 5.32 kgm. These dimensions, striking as they are, have been considerably surpassed by some found in English and American literature. Eddowes[10] mentions the birth of a child weighing twenty-two pounds two ounces. The mother was thirty-three years of age, and had previously borne two children of large size. Chubb[11] met with one case in which the child weighed twenty-one pounds. The other children of the family were exceptionally large. The fact that some women have a tendency to bear large children is also well illustrated by an observation of Dickinson's,[12] where a woman was delivered by craniotomy and evisceration of a child weighing sixteen pounds. Her first child weighed nine pounds and her second twenty. Beach[13] records the birth of the child of Captain Bates and Anna Swann, both of gigantic proportions, which weighed twenty-three pounds twelve ounces. Baldwin[25] quotes the case of a woman who after having three miscarriages finally had a child weighing twenty-three pounds. There are at least ten other instances on record of new-born children weighing from thirteen to twenty pounds. The largest child I have been able to find recorded is a case of Dubois,[15] which attained the almost incredible weight of 11.3 kgm. (24 pounds 13¼ ounces).

As will readily be understood, the fate of giant children is often an untoward one. Not infrequently they die in the later months of gestation. When brought to term, they have to be delivered by operative interference of some kind, and are often still-born. It is an interesting fact that the dystocia is brought about, not by the head, which usually, unless hydrocephalic, does not exceed in size that of a normal child, but by the size of the trunk. The biacromial diameter is excessive. In Dubois' series of forty-four cases only twenty-six were born alive. Children of 8 kgm. and over are invariably still-born. In those that survive, the excessive size at birth is sometimes compensated for by slow growth subsequently, but the pathological nature of the process is sufficiently indicated by the fact that such children often grow very fast and attain puberty in the third to the sixth year. It is perhaps questionable whether all cases of precocious development, wherein the individual attains the structural and functional characteristics of the adult in early childhood, are to be regarded as manifestations of gigantism. Some at least have this in common with gigantism that they show evidences of early senility. Development is rapid and decay is premature. Phlegmon ("De Mirabilibus," cap. 32) is the authority for the statement that Craterus, the brother of King Antigonus, was an infant, a young man, married and begat children, and became an old man in the short space of seven years. In 1741 a boy was born at Willingham, near Cambridge, who when twelve months old presented all the appearances of puberty and died an old man at the age of five years (Philos. Trans. of the Royal Soc. of London). The subsequent history of unusually large children is unfortunately not often to be traced, but there is some slight evidence to show that they may develop into gigantic adults. Bonardi[16] reports an interesting case which throws some light upon this point. A boy at the age of fifteen had the size and development of an adult male. At twenty-two he began to suffer from pains in the head with nausea, and soon after the hands, feet, maxillæ, and tongue began to increase in size. At the age of twenty-nine he measured 194 cm., and presented all the signs of acromegaly. In other instances, too, the abnormal increase in size has been known to begin quite early. Gilbert of the Hôpital Broussais (quoted by Meige, *loc. cit.*, p. 449) met with an individual who began to grow rapidly after an attack of some acute fever in his earliest infancy and eventually attained the height of 196 cm. The American giant Wilkins began to grow rapidly at the age of four, and reached his full height (245 cm.) at eighteen. As a rule, however, the excessive growth does not become in evidence until some time between the tenth and twentieth years, usually with the onset of puberty.

The student of ancient lore will be interested and amused to see how superstition and the love of the marvellous have combined to render many of the accounts of giants that have come down to us thoroughly unreliable. Judging from these stories, the height to which the human race may attain has varied between wide limits. Pliny, like Augustine, believed that the stature of mankind had deteriorated, but this is not substantiated by the examination of such ancient remains as we possess. The rabbinical legends teem with incredible accounts of the height of the various Biblical characters. Adam's height was calculated to be one hundred and twenty-three feet and Eve's one hundred and eighteen. According to the Biblical account the bedstead of Og, King of Bashan, was nine cubits long. Pliny mentions the giant Gabbaras, between nine and ten feet high, who was brought from Arabia by the Emperor Claudius, and states further that the remains of Posio and Secundilla, found in the Sallustian Gardens in the time of Augustus Cæsar, measured each ten feet three. Josephus refers to a Jew nearly eleven feet high, who was sent as a hostage to Rome by the King of Persia. Some remarkable stories are told of the Emperor Maximin (C. Julius Verus Maximinus) who was born in 173 in one of the frontier villages of Thrace. A shepherd in his youth, he soon became noted for his extraordinary height and strength. He took part in the games given by Septimus Severus to celebrate the occasion of the birth of his son, and overcame sixteen of the most powerful wrestlers without taking breath. The Emperor attached him to his own person and he was made a centurion by Caracalla. Capitolinus says that he was a finger's breadth over eight feet in height. His thumb was so large that he could use his wife's bracelet for a ring. He stopped a wagon with one hand, broke the jaw of a horse with a blow of his fist, and could break its leg with a kick. He is credited with eating forty pounds of meat in a day and used to drink as much as a Capitoline amphora (about twenty-six litres). He became tribune under Alexander Severus, and, conspiring against him later, was elected emperor. He reigned for three years, execrated for his cruelty, and was finally assassinated by the soldiers in 238.

Coming to more recent times, we have some equally extraordinary tales brought back by travellers. Magellan is said by some to have given the name Patagonia to the country he discovered because its inhabitants measured five cubits. Lemaire, in describing his voyage in 1615 to the Straits of Magellan, states that at Port Desire he found several graves covered with stones in which were skeletons of men measuring from ten to eleven feet. More recent travellers have, however, found the Patagonians to be not excessively large; in fact many of them are rather diminutive. The naturalist Turner believed that he saw on the River Plata near the coast of Brazil savages twelve feet high. Accounts more marvellous still are given of giants from nineteen to thirty-six feet high, who have existed at various times in Europe. These are based on the discovery of bones of prodigious size, which were erroneously regarded as human. In

those days nothing was known about comparative anatomy, and the remains in question were no doubt those of some of the lower animals. Sir Hans Sloane, in an elaborate and learned disquisition on the subject, came to the conclusion that the bones referred to were parts of whales, mastodons, elephants, or other enormous beasts, although he thought that some of the stories could not be entirely discredited. It is a fact, however, that in more recent times, when such matters are much more narrowly scrutinized, no such instances of excessive height can be substantiated. Buffon, the great naturalist, usually a reliable authority, had no doubt that human beings had existed who were from ten to fifteen feet high. It is not until we come to the eighteenth century that we get reliable data as to the height of giants. According to Dana[16] not more than a hundred giants have been exhibited in public since 1700, and of this number only about twenty were said to have been over eight feet. Topinard measured the tallest man in the Austrian army, and found him to be eight feet four and a half inches. Winckelmeyer was eight feet six inches. Marianne Wehde, a more recent German giantess, was eight feet four and a half inches when sixteen and a half years old. In view of these observations we must seriously question whether any human being has ever exceeded nine feet in height. Quite a number of giants have been recorded who measured between seven and eight feet, but above this limit the cases are extremely few. The history of these is often extremely interesting. Queen Elizabeth's porter, whose portrait, painted by Zucchero, is now in Hampton Court Palace, was seven feet six inches high. Walter Parson, the porter of James I., was as big. William Evans, the porter of Charles I., was about eight feet high. Cromwell's porter, Daniel, who died a lunatic, attained the height of seven feet six. In the reign of George I., an Englishman, seventeen years old and eight feet tall, was exhibited at the Bartholomew Fair at Smithfield. "Big Sam," the porter at Carleton Place when George IV. was Prince of Wales, was eight feet in height. In a Dutch village in 1712 there died a fisherman called Gerrit Bastiaansen, who measured eight feet and weighed five hundred pounds. As a contrast to this we may cite a giant who was exhibited at St. Petersburg in 1829, who measured eight feet eight, but withal was thin and emaciated.

One of the most celebrated giants was Cornelius McGrath, whose skeleton is now in the museum of Trinity College, Dublin. He was born in 1736 in the county of Tipperary. His parents and the other members of the family were of ordinary size. After the age of fifteen he began to suffer from violent pains in the limbs and began to grow rapidly. At the age of sixteen he was six feet nine. In 1753, six months later, when he first exhibited in public he measured seven feet three inches in his stocking feet. It is said that he was ungraceful in appearance, of low intelligence, and spoke in a childish manner. He died at the early age of twenty-four. His skeleton measures seven feet eight inches.

John Middleton, called the "Child of Hale," was born in 1752 at Hale in Lancashire. His portrait is preserved in Brazenose College. He is said to have measured nine feet three inches.

O'Brien or Byrne, the "Irish Giant," is celebrated not only for his great height, but for his connection with the distinguished anatomist John Hunter. Hunter was particularly anxious to secure his body and made the most extraordinary exertions to obtain it. O'Brien was aware of this desire on the part of the anatomist and was correspondingly averse to being "set up" as a specimen. Shortly before his death, which occurred at the age of twenty-two, O'Brien bribed some of his friends to take his body, and after weighting it with lead to sink it in the sea. The undertaker, however, who had been previously interviewed by Hunter, managed to have the coffin locked up in a barn while the escort was refreshing at an inn. Thereupon some men, stationed there for the purpose, substituted an equal weight of paving stones for the body which was forwarded that night to Hunter. He took it in his carriage to Earl's Court, where it was immediately prepared. It is estimated that it cost nearly five hundred pounds to secure the body. O'Brien is said at the time of his death to have been eight feet four inches high. His skeleton, however, measures only seven feet seven. It is now, together with the kettle in which the body was boiled, in the museum of the Royal College of Surgeons in London.

The successor of O'Brien, Patrick Cotter, who for a time exhibited under his name, was born in 1771. At his death, which occurred at the age of forty-five, he is variously estimated to have been from eight feet one to eight feet seven in height. At one time he was examined by Dr. William Blair, who found him to measure about seven feet ten. He was badly proportioned, and looked like a weakly or even imbecile person. His forehead was low, his pulse feeble, his voice weak, and he suggested in appearance a sickly child that had grown too fast.

Robert Hale, the "Norfolk Giant," who died at Yarmouth in 1843 at the age of forty-three, was seven feet and a half high and weighed four hundred and fifty-two pounds.

Among the better known of the exhibited giants were Captain Bates, of Kentucky, and his wife, Anna Swann, of Nova Scotia. Captain Bates enlisted in the Southern army at the beginning of the American Civil War, being readily accepted on account of his size, although he was only sixteen years of age. By the end of the war he had attained the height of seven feet two and a half inches. He gradually increased in weight also until he turned the scale at four hundred and fifty pounds. While in England in 1871 he married at St. Martin's-in-the-Fields Miss Anna Swann, who measured seven feet five and a half inches. On neither side were the parents of more than ordinary stature.

Chang, a celebrated Chinese giant, died at Bournemouth in 1896, at the supposed age of fifty-one. He was upward of eight feet high.

At the Alhambra in London in 1882 was exhibited the "Queen of the Amazons," who was eighteen years old, and measured eight feet and half an inch.

We owe much of our present knowledge of the processes of growth and development to the epoch-making work of Winslow, Haller, Meckel, and the Saint-Hilaires, father and son. Although of late the interest of scientific men has been somewhat revived in the subject we cannot as yet be said to have made much advance, except that we are beginning to apprehend more fully the nature of the problems involved. We are now realizing the fact that growth and development are a very complicated matter. We see, for instance, that we must draw a distinction between mere growth, or what may be called vegetative force, function, and reproductive power. These three factors are more or less correlated, but the correlation often varies both in kind and in degree. Certain cells are specialized for growth, others for function, others for proliferation. All cells may at some time in their life history be specialized in one or other of these directions according to the demands made upon them, but they cannot be specialized in all three directions to the same extent at the same time. Thus a cell that is about to divide ceases to grow and enters into a resting stage before mitosis occurs. And other illustrations might be given. Moreover, what is true of the cell is true of the community of cells known as the individual. Up to a certain period of life the forces of the body are concentrated toward the main object of growth. Later, function becomes more in evidence. Last of all the power of reproduction becomes established and perfected. In gigantism disturbance of growth in the direction of increased stature and weight is the predominant feature, but, as we shall see, this does not occur as a rule without exacting a corresponding penalty in the degradation of the general bodily functions and the power of reproduction. The causes which lead to this result may be inherent in the germ cells so that they make their influence felt quickly in the construction of the organism,

or they may become operative subsequently to fertilization and segmentation of the ovum, either during intra uterine life or after birth. These influences may, further, be exerted upon the body as a whole or on some part of it. There is therefore a family relationship between gigantism, dwarfism, and the various malformations and monstrosities. In both dwarfism and gigantism, which are not, as might at first sight be supposed, perfect opposites one of the other, there is not merely an inhibition or an exaggeration of the normal processes of growth, but in the vast majority of cases something more, namely, a perversion of growth. In the normal infant at birth, the head and trunk, but particularly the head, are relatively large. As the time of puberty approaches the picture changes. Growth is rapid and irregular. The limbs are now disproportionately large, the hands and feet being especially prominent. To use a common expression the child has become the hobbledehoy. Only in the later period of puberty does the trunk enlarge, the figure consolidate, until the perfect proportions of the adult are attained. There is a striking parallel between the hobbledehoy stage and what we find in gigantism. In giants the exaggeration of growth is also disproportionate and irregular. The head is often small, or at least about the same size as the head of a normal youth or adult of the same age; the increase in height is mainly due to the excessive growth of the lower extremities as compared with the rest of the body. Here, however, the parallel ceases. Giants are often weakly rather than strong; the sexual organs are apt to be badly developed, and the sexual proclivities are sluggish or delayed. They are liable to contract disease and show signs of premature senility; in fact they rarely reach middle life. Dwarfs, on the contrary, are long-lived. They frequently have the relatively large head of the infant, with evidences of delayed ossification of the cartilages, and genital inadequacy, facts which have caused many to regard dwarf growth as really infantilism. Unlike the giants they frequently possess average or more than average mental powers. It is clear that in both gigantism and dwarfism the disturbance, whatever it is, manifests itself mainly in the rate and extent of the growth, but still to a noteworthy degree in disordered function. And it is not merely the process of ossification that is at fault but the body as a whole—bones, soft parts, and internal organs—is involved. Nevertheless the disturbance of ossification appears to be the controlling force, for it undoubtedly dominates the picture.

Normally, the growth of bone depends on the activity of certain specialized cells—the osteoblasts—which are chiefly situated in the deeper layers of the periosteum, at the extremities of the bones, and along the interosseous sutures. Growth in thickness takes place from subperiosteal osteoplasia; growth in length is due to the influence of the osteoblasts in the spongy ends of the bones and in the epiphyseal cartilages. Inhibition or exaggeration of stature is due in the main to dystrophic changes at the extremities of the long bones, although subperiosteal osteogenesis is also to some extent interfered with. The results depend not only on the inherent vegetative forces at work in the cells, but on the condition of the epiphyseal discs. So long as the discs are movable, growth in length of the bone is possible. This is interestingly borne out by recent investigations with the *x*-rays in certain forms of anomalous growth. Joachimsthal[17] found in some lilliputians that he examined that the bone formation was delayed, and the condition of the discs and of the bone generally was strictly comparable to that found in the child, although the subjects were in the neighborhood of thirty years of age. Hofmeister[18] also in cretinism found that the epiphyseal discs persisted for a long time, and that the epiphyseal ends of the bones grew slowly. In chondrodystrophia fœtalis an ingrowth of periosteum has in some cases been observed between the disc and the end of the bone. The significance of this is not quite clear. In acromegaly, on the contrary, where the increase of size of the bones, still at the distal ends, is in breadth and thickness, rather than in length, there is complete union or synostosis of the epiphyses. With regard to giants we unfortunately have no information on this point, but I think we may fairly infer that, while growth is in excess, epiphyseal synostosis is delayed. The importance of the condition of the epiphyseal discs in modifying the extent and the direction of the growth is also prettily illustrated by the observation of Lorain, who found in some cases of dwarfism premature ossification and union of the epiphyses.

In our discussion of growth and its anomalies so far we have contented ourselves mainly with freeing the subject from entanglements, and so to speak preparing the ground for action. When we come to consider the more remote factors concerned in the question of growth we find ourselves in a much more difficult position. As we do not know what life is we can apprehend its methods and its manifestations only in an imperfect way. Many of our ideas, therefore, have to be based upon inference rather than direct proof.

The part played by heredity in gigantism, as in other anomalies of development, is of considerable interest and importance. This factor might be expected to be more prominent in cases of congenital gigantism, and as a matter of fact it is so, but its influence cannot be overlooked in the other forms. It is a matter of common observation that parents transmit their tendencies and peculiarities to their offspring, and moreover these peculiarities may be traced through several generations; in fact they may become familial or racial characteristics. This law manifests itself in many ways, in the size and configuration of the body, in the color of the skin, the mentality, habits, the susceptibility to disease, and in many minor traits. The peculiarities derived from the paternal and maternal sides may be of such a nature as to neutralize one another, or again they may unite their forces to produce an exaggerated effect, an effect so pronounced as to be marked at once as an anomaly. With regard more particularly to gigantism, we do not meet with the anomaly as a racial characteristic at the present day. At most we can say that some races tend to be tall and large, while others are small or even dwarfed. If the ancient accounts are to be believed giant peoples have, however, existed. Whatever stress we may lay upon this, at the present time gigantism is a sporadic affection. It is a suggestive and striking fact that once the tendency toward gigantism is acquired it is apt to crop out at various times in the same lineal descent, exemplifying the law of atavism. Again it may often be noted that more than one of the children of the same household will be affected. A number of cases might be quoted to illustrate these points. In Dickinson's case (*loc. cit.*) mentioned above, a woman bore three children who weighed nine, twenty, and sixteen pounds respectively. Fuchs' case (*loc. cit.*) was a IX-para. Her sixth child weight 6 kgm., her eighth 6.1, and her ninth 7.55. Her other children had also been heavy. The same thing has been noted by other observers. Goulart refers to a Polish giant who was exhibited in Paris in 1571, and was so tall that in a lofty room he could touch the ceiling with his head. He was married and had a son who promised to be as tall as he was.

James Toller, exhibited in London in 1815, was seven feet nine inches high. His parents were of normal build, but he had two sisters of gigantic stature. Louis Frenz, a French giant, who was born in 1800, and measured seven feet six, had two sisters as tall as he was and one brother who was much larger. The family history of Robert Hales, "the Norfolk giant," is also quite striking. His father was six feet and a half, his mother six feet, in height. One of his ancestors, who lived in the reign of Henry VIII., measured eight feet eight inches. Hales had five sisters who averaged six feet three and four brothers who averaged six feet six. The tallest of the sisters died at the age of twenty, measuring seven feet two. Captain and Mrs. Bates, both over seven feet, had a child which is almost the largest on record. One of the sisters of Chang, the Chinese giant, was even taller than he was, measuring eight feet four.

These facts suggest that this anomaly of growth is due

to peculiarities inherent in the germinal cells of the parents. This view is supported by the observations of Engel-Reimers,[19] who has emphasized the fact that excessive muscular development, the so-called "athletic habitus," appears to be due to an abnormal hereditary predisposition and not to hypertrophy from functional overactivity. This is well borne out by the physical condition in new-born giant children. They frequently present the athletic habit. The head is about the size of that of the normal infant, but the trunk is massive. Now this hypertrophy, if we can call it such, is clearly not due to mechanical work nor to compensation, nor to the other ordinary causes of overgrowth. It must be due to some disturbance of nutrition. The relative importance to be attached to peculiarities of the male and female germ cells is still in doubt, for in the recorded cases we rarely have any statement as to the physical condition and development of the father. From the instances cited it is evident that both germinal elements may play a part. But it is equally evident that some idiosyncrasy in the maternal organism alone is sufficient to produce the result. In Fuchs' case, for instance, the father is noted as having been in a poor state of nutrition. This has led Werth to suggest that the tendency to produce large children is due to an inherent peculiarity of the ovum, possibly to its large size. However this may be, we have sufficient evidence to show that large size on the part of one or both parents is not necessary to produce the result in question. Yet it seems probable that physical superiority in the mother, if not in height, at least in physical constitution and nutrition, is an important etiological factor. In 178 cases of large and giant children collated by Fuchs, 166 mothers are noted as being of more than usually strong physical development and nutrition. The remaining 12 were weakly, but in no case did their children exceed 4.36 kgm. in weight, a size which, according to our adopted standard, cannot be regarded as gigantic. In view of this fact we see that the influence of maternal development and nutrition assumes considerable importance. Exceptions to this, however, occur. In a case cited by Dubois, a woman with extensive tuberculosis gave birth to a child weighing 6.336 kgm., and another with severe diabetes had a child of thirteen and a half pounds. Two possibilities must evidently be considered in this connection, a primary peculiarity of the ovum or sperm cell, or both, and a condition of increased intra-uterine nutrition. The influence of peculiarities of the primitive germinal cells would perhaps be best illustrated by instances of the atavistic manifestation of gigantism, or in those cases, like that of Dubois, in which the maternal organism was conspicuously weak, for in the latter case increased intra-uterine nutrition could obviously play no part. Some of the forms of minor terata, such as polydactylism, are no doubt also of this nature. Polydactylism has been known to run through a family for three, four, or even five generations, being eradicated only in process of time by marriage with normal persons. Curiously enough polydactylism has been found associated both with dwarfism and with gigantism. It has been thought by some that mothers in whom the function of menstruation was established early were more likely to have larger children than others, apparently on the theory that such persons were possessed of greater reproductive energy. Negri on the basis of 333 observations has stated that the children of mothers who began to menstruate early were both larger and heavier than the offspring of those whose menstruation was late in coming on. This has not been confirmed, however, by other observers. The point can probably not be decided until more studies on the subject are forthcoming. It is, nevertheless, true, so far as the records go, that large children are more likely to be borne by those who are at the height of reproductive activity and who have had previous children. In elucidation of this point we may perhaps quote Fuchs' statistics. In 176 of his cases, already referred to, the age was ascertained. These were divided as follows: I. Under twenty years, 5; of this number 5 were primiparæ. II. Twenty to twenty-five years, 72; of this number 18 were primiparæ. III. Twenty-six to thirty-five years, 75; of this number 2 were primiparæ. IV. Thirty-six to forty-eight years, 24; of this number none were primiparæ.

Between the ages of twenty and thirty-five, the years of the greatest sexual activity, the number of large children was greatest. Now, taking the third class, we find that only 2.6 per cent. were primiparæ. If these results be compared with those obtained from a series of 1,000 normal births, in 342 of which the mothers belonged to the third age period, it will be found that there were 57 primiparæ, a proportion of 16.9 per cent. This corroborates the observation made a little while ago that certain women show a tendency to produce large children, or in other words that the tendency once manifested tends to perpetuate itself.

Intra-uterine nutrition is undoubtedly a factor of considerable importance. In the article on *Dwarfism* or *Nanosomia* in this volume the rôle played by intra-uterine malnutrition in the causation of inhibited growth is dealt with at some length. Here syphilis, alcoholism, and tuberculosis, together with lesions resulting in interference with the free circulation of blood through the placenta, are of importance. Conversely, an overplus of nutritive energy might be expected to produce its effect upon the fruit. In this connection we have to take into account the condition and surroundings of the mother during pregnancy. Pinard (cited by Bouchacourt[20]) compared the average weight of 500 new-born children whose mothers had worked up to the time of delivery with that of the same number of children whose mothers had rested during the later weeks of pregnancy. He found a notable superiority in weight and nourishment in the offspring of the latter class. In a similar inquiry Bachimont (cited by Bouchacourt) in a series of 4,445 observations found the excess in weight for the latter class of children to be, on the average, 300 gm. In this particular it should be remarked that very large children lead perforce to a condition of complete inactivity and inertia on the part of the women pregnant with them. This of course means rest which tends to increase in turn the size of the child. Thus a vicious circle is induced. The importance of intra-uterine nutrition in modifying the weight of the fruit is well illustrated by the good effect of dieting in those cases in which a woman has either a tendency to produce large children or else has some contraction of the pelvis. By this procedure it has been found possible to deliver such a mother of a living child.

Some attention had been directed to the subject of prolonged gestation and its effect in producing large children. The statistics seem to show that this factor has a certain amount of importance, but it is probably effective only when combined with other causes. It does not seem to me, however, that it is justifiable to place cases of this kind in the same category with giant growth. If, for example, a child is retained within the uterus for three hundred and eight days instead of two hundred and eighty, it is practically in the same position as an infant one month old, due allowance being made for differences between intra-uterine and extra-uterine modes of nourishment. Such a child would derive no permanent advantage from its prolonged retention within the uterus, and would probably develop later much as other children do. In other words, the vitium of excessive growth is not inherent. Unfortunately many of these points we have touched upon cannot be verified by any large series of observations. Gigantism in the first place is much rarer than dwarfism. Then the majority of giant children are still-born. Even those cases in which giant growth manifests itself later in life are beset with difficulties. The number of carefully made studies is not great and prolonged observation is rarely possible, not only from the fact that giants are apt to die early, but on account of their nomadic kind of life.

In dealing with the question of heredity we have adduced numerous facts to show its importance in the causation of anomalous forms of growth. The influence of

this factor, while perhaps more direct and striking in the case of giant births, is nevertheless, as we have shown, to be taken into account in the post-natal forms. But besides this we have to consider the bearing of internal metabolism on the subject. The more recent work done on cretinism and the results of the experimental removal of the thyroid gland have taught us that a condition of athyroidea, which undoubtedly acts by perverting the metabolic processes of the organism involved, has a profound effect on the function of growth and development, namely, in the direction of inhibition. In that other most remarkable perversion of growth, acromegaly, where there are enlargement and deformity of the body, or excessive growth, gross lesions of the pituitary body have been found. Disorders of internal secretion obviously are of some importance.

The general resemblance between acromegaly and gigantism has led to the promulgation of the view that the two conditions are one and the same thing, and the controversy over this point has waxed hot and heavy. Without being prejudiced on either side, I think that the careful observer cannot fail to be impressed with the parallelism which exists between the two affections. Brissaud and Meige have been the chief exponents of the identity theory, while Marie, who first differentiated acromegaly as a disease entity, though he has somewhat receded from his first position that acromegaly and gigantism are entirely distinct, has not been entirely convinced by the arguments adduced against his position.

Marie in his first studies on acromegaly summarized it as a peculiar affection, characterized by a massive hypertrophy of the bones of the extremities and the extremities of the bones. He admitted that a number of cases had been confounded with gigantism, for the reason that attention had been directed to the excessive height to the exclusion of the less obtrusive signs, while the disease in those of normal stature had been overlooked. Shortly after, Guinon,[22] following Marie's lead, took the same position that the two affections were essentially different, on the ground that as our knowledge had increased it had to be recognized that persons with acromegaly were by no means always gigantic; in fact they were often below the average height, and again that the configuration of the body was different in both. The various parts of the face and limbs preserved their normal proportions in gigantism while the course of the two affections was different. Guinon even went so far as to state that gigantism is as a rule simply an exaggeration of a normal process, while acromegaly is a disease. It is undoubtedly a fact that typical, or what we might call "text-book" cases of the two affections present an entirely different picture. There have been some giants that presented none of the morphological characteristics of acromegaly, as there have been persons with acromegaly that were not giants. It ought to be unnecessary, however, to point out that even the best-known diseases present at times wide variations from the type. The case of typhoid fever, for instance, need only be mentioned. This being the case it by no means follows that two diseases, at first sight dissimilar, have nothing in common, or even that they are not due to the same cause. The point may be further illustrated by the history of cretinism and myxœdema. At one time it was believed that these conditions, which in many ways are so unlike one another, at least to superficial examination, were distinct diseases. More careful study has, however, shown that both depend on a condition of athyroidea, and few will be found now to deny that cretinism and myxœdema are one and the same thing. The modifying factor has been found to be the age and the concomitant stage of development of the affected individual. If athyroidea becomes manifest in infancy before the bony skeleton is consolidated we get cretinism. If it develop later, when the bony skeleton is complete, the soft parts only are involved and we get myxœdema. It is unsafe then to conclude that one and the same cause may not at times produce widely different results. In other words, the trophogenic function of the individual may be so predominant that it is sufficient to alter a morbid state almost beyond recognition. It has already been pointed out that the normal process of growth manifests itself most strongly at the epiphyseal ends of the long bones, and that increase in length of the bones is possible only so long as the epiphyseal discs remain ununited, save by the softer structures, to the diaphyses. Similarly, the abnormal processes of growth, such as dwarfism and gigantism, manifest themselves at the same points. Deficient vegetative energy in early life will result in stunting the growth of the long bones, and the same thing will happen if the epiphyseal cartilages are prematurely ossified. Excessive vegetative power during adolescence results in increase in height; if synostosis of the epiphyses has taken place, as occurs in adult life, then it is conceivable that, increase in length being impossible, increase in breadth and thickness must occur. Do, then, acromegaly and gigantism bear to one another a relationship similar to that existing between myxœdema and cretinism? Many facts point in this direction. Numerous observations have shown that acromegaly frequently supervenes in gigantism. Surmont[23] in 1890 reported a case of acromegaly in a girl of eighteen, in whom the symptoms were preceded by a notable increase in the size of the body. The enlargement was generalized, but most marked at the extremities. Byrom Bramwell[24] mentions the case of a giantess who was attacked by acromegaly. Swanzy[26] also demonstrated the lesions of acromegaly on the skeleton of McGrath, the Irish giant, before the Royal Academy of Medicine of Ireland. Shattock[27] believed the skull of O'Brien to be acromegalic. In 1893 Dana[16] published two cases of acromegaly associated with gigantism, and he remarks that the coincidence of the two affections is more common than has usually been supposed. He further mentions a great many symptoms which they have in common, and brings out the most important point, viz., that out of twelve autopsies on giants the pituitary body was enlarged in ten. In the case of "Adma," a French giantess, who died at the age of twenty-one, measuring six feet eight and a half inches, Hutchinson states[28] that the face and extremities presented the well-known features of acromegaly At the autopsy the pituitary gland was found to be considerably enlarged. A striking case, also, is reported by Brissaud and Meige.[21] J. P. Mazas, the giant of Montastruc, began to grow rapidly when thirteen years of age, and became very strong and robust. At twenty-one years he was 212 cm. high, eventually reaching 220 cm. At the age of thirty-seven he experienced a severe pain in the back, which he attributed to lifting a heavy weight. Deformity of the back set in and his height began to diminish. He gradually developed enlargement of the face and extremities, headache, weakness, intellectual and sexual torpor, and all the classic symptoms of acromegaly. Sternberg,[29] also, in an elaborate paper on the subject found signs of acromegaly in forty two per cent. of giants. More recently Walker[30] reported an instance of acromegaly in a boy, who began to grow rapidly when six years old, and who at sixteen was six feet five and a third inches high, and weighed two hundred and forty-five pounds. Bonardi[15] refers to the case, already mentioned in another connection, of a boy who at the age of fifteen had the size and development of an adult male. When twenty-two years old he began to suffer from pains in the head and nausea. Soon after, general weakness set in, with enlargement of the hands, feet, maxillæ, and tongue. At twenty-nine he was 194 cm. high and was typically acromegalic. By a careful study of the recorded cases we see, therefore, that a considerable degree of parallelism exists between the two affections. Perhaps the most important points are to be noted in the skeleton.

The typical features in acromegaly are enlargement of the bones of the face and extremities. The hands are "spade-like," and the fingers rounded. In severer cases all the bones of the body become involved. The thorax enlarges and the trunk becomes scoliotic, so that a loss of

height takes place. There exist, however, lesser disturbances of bone formation that are difficult to class, being on the border line between gigantism and acromegaly. In such cases the dystrophic disturbance is confined to one or more parts of a member, or to two members symmetrically. Such malformations may be both congenital and acquired. Of such a nature are those cases in which there is deformity of the face without enlargement of the hands. Chauffard[31] reports a case in which a man of thirty-two presented the features of prognathism, macroglossia, prominence of the external occipital protuberance, headache, anæmia, loss of vision to the right, and slight kyphosis. Some of the anomalies, then, that are to be found in acromegaly may be found without the other features of the disease in certain forms of developmental dystrophy, and may arouse a suspicion as to the acromegalic nature of the case. When such peculiarities are met with in giants we may properly inquire whether they are the stigmata of acromegaly, or whether they merely simulate that disease. In giants thickenings of the extremities of the long bones, hyperostoses, and exostoses have been noted, identical with those that for so long have been regarded as characteristic of acromegaly. Deformities of the knees, which as Osborne, Middleton, Schultze, Hitschmann, and Roswell Park have shown, are fairly common in acromegaly, have also been met with in gigantism. Lucas Championnière in 1899 demonstrated to the Academy of Medicine a giant, aged twenty-seven, who measured 203 cm., and presented an extreme genu valgum. This peculiarity has a double interest in that it affords a link between acromegaly and gigantism, and also connects the latter with infantilism. The curvature of the spine and the rounded thorax, so often found in acromegaly, have been found in gigantism, but our information is defective in this regard.

With respect to muscular power great variations may occur both in gigantism and in acromegaly. Several observers, notably Meige, Dallemagne, Virchow, P. Marie, Souza-Leite, Bourneville, and Regnault, have noted acromegaly developing in persons of exceptional muscular vigor. Some giants, like the Emperor Maximin and the Countess Lodoïska, have been of great strength. This, however, seems to be the exception. Geoffroy Saint-Hilaire states that giants are "without activity, without energy, slow in their movements, avoiding work, quickly fatigued; in a word, feeble in body as well as in mind." Amyasthenia and general weakness are by no means uncommon in acromegaly.

As is well recognized there is a characteristic facies in acromegaly. Meige is our authority for the statement that giants who are still in the period of growth present no special facial peculiarities. In those who have ceased to grow there is an exaggerated development of the face as compared with the cranium. We can sometimes note that the malar eminences are prominent, the lower jaw enlarged, and the angle widened, while the lips are thick. The beard is often thin, the skin thick and dark, the pupils dull, and the whole appearance lacks vivacity. These peculiarities are by no means invariable in giants, nor indeed are they so in acromegaly. We have to allow here as elsewhere for individual variations. In fact, we may perhaps with Hoffmann distinguish between acromegaly of the soft parts and acromegaly of the bones.[32] Meige is, on the whole, inclined to believe that the face in giants at one time approaches the acromegalic type, at another the infantile.

Vascular disturbances have been found in both acromegaly and gigantism. In both the pulse is slow, the circulation sluggish, and there may be varices.

Pains in the head have been found in both affections. Pains also in the limbs, vertebral column, and the viscera, have been met with in about half the recorded cases of acromegaly. These may simply amount to a sense of fatigue or lameness, but may be actually articular, muscular, or neuralgic. It is a popular belief that rapid growth in children is associated with "growing pains," and it is interesting that the same thing has often been noted in giants. In the case of McGrath, for instance the increase in growth was associated with the most violent pains in the limbs.

Visual disorders have been met with both in acromegaly and in gigantism. In acromegaly, at least, they have been found to be dependent on the presence of a tumor of the pituitary body.

Polydipsia, polyphagia, and abundant sweating have been observed in both affections. Polyuria and glycosuria are occasionally met with in acromegaly and in giants who become acromegalic.

In both gigantism and acromegaly there is often to be noted sexual frigidity in the male, and amenorrhœa in the female.

To sum up, the two affections frequently have the following symptoms in common: asthenia in the widest sense of the term; muscular weakness, notwithstanding the absence of atrophy; intellectual degradation; melancholy; headache; diminution of sexual desire in the male; amenorrhœa in the female; alterations in the skin; varices. Lastly, of a great importance, lesions of the pituitary gland have been found in a majority of both affections.

Further, the influence of heredity is marked in acromegaly as in gigantism, and indeed it is not uncommon in probing into the family history to find that acromegaly and gigantism are liable to be met with in the same family. Schwoner, for instance, records[33] a case of acromegaly in a woman of forty-five, whose mother had become acromegalic at fifty. All the members of the family on both sides of the house are noted as having been of great stature. Lackey[34] describes a case of acromegaly in a negro who reached the extraordinary height of eight feet six. His grandfather is said to have been a giant.

In view of the facts outlined above, Brissaud and Meige would discover a general principle underlying the dystrophic disturbances that result in excess. Growth at all periods of life tends to be manifested most conspicuously at the epiphyseal ends of the long bones. The effect produced is controlled by the age of the patient, or, in other words, by his vegetative capacity and the condition of his epiphyseal cartilages. The same pathological process which in the young gives rise to gigantism will, if continued after the normal period of growth in stature is passed, cause acromegaly. If it becomes operative in later youth, when the bones are largely formed but growth is not complete, we get a combination of acromegaly with gigantism. This is to some extent corroborated by the lesions in acromegaly, for, as Marie himself has shown, in cases of acromegaly that begin early in life, the extremities are more elongated than thickened, and are quite unlike the spade-like extremities characteristic of the disease as it occurs in later life. Further, it may be safely stated that acromegaly has never preceded gigantism, while acromegaly has succeeded gigantism in almost half the cases. Brissaud and Meige, however, would go further. They see the same principle at work in the chronic rheumatism so-called of the aged, in rheumatoid arthritis and gout; in youth, in gigantism; in adult life, in acromegaly; in old age, in nodes. They support this by an observation made by Gaston and Brouardel[35] with the x-rays on a woman of sixty, who began to show signs of acromegaly at forty-two after the menopause. The disease was slowly progressive, and thickenings in the form of nodules could be made out on the epiphyseal lines.

Without endorsing the rather startling proposition put forth by Brissaud and Meige, that "acromegaly is gigantism of the adult; gigantism is acromegaly of adolescence," it seems to me that the unprejudiced observer cannot fairly deny that they have proved their main contention. There is undoubtedly a close connection between acromegaly and gigantism, and the two affections in a large proportion of cases merge gradually one into the other. Gigantism frequently becomes acromegaly. But how about the other fifty-eight per cent. of cases of gigantism that present no signs of acromegaly? Are these, too, of the same nature, or are they in a different category? It is not impossible nor even unlikely that

some of them are due to the same factors as acromegaly, as it is ordinarily understood. Here we have to consider the natural variations of disease. Diseases do not invariably run their course. They may become ameliorated or may be aborted. Acromegaly itself may present an extremely slow progression, and in fact may cease to advance. A fatal termination does not always occur. It may well be, therefore, that acromegaly beginning in early adolescence may progress only sufficiently far to produce increase in length of bone without the other signs supervening. It may be recalled in this connection that the majority of giants die early. Byrne, the Irish giant, died at twenty-two; James Toller at twenty-four; the "Queen of the Amazons" at about twenty. This may perhaps be the effect of the acuteness of their malady, but in many cases it is due to intercurrent disease, as the resisting power of giants is notoriously low. However this may be, it is plain that many giants die before the period of age incidence of acromegaly, that is to say, before adolescence is completed. We cannot therefore say that they would not have become acromegalic had they lived. It is possible, therefore, that the majority of the cases of gigantism are dependent on the same pathological factors as acromegaly.

There has been considerable debate as to the exact nature of the cause or causes at work in acromegaly. Klebs advanced the theory that acromegaly is due to angiomatosis. Vascular lesions are undoubtedly present both in acromegaly and in gigantism. Witness the arteriosclerosis, the varices, the vaso-motor ataxia, and the hypertrophy of vessels to adjust themselves to the increased size of the body. But there is no proof of any new formation of vessels. Lancereaux, again, has suggested that it is a trophoneurosis. The enlargement of the hands and the disturbed innervation met with in syringomyelia might suggest this. This view is not, however, supported by any known facts. von Strümpell has thought that it is a congenital dystrophy. The majority of observers are, I think, practically agreed that acromegaly is dependent on some gross lesion of the pituitary body, in the form of hypertrophy, cystic growth, adenoma, or other tumor growth. Osborne believes that gigantism in its perfect development is due to a normal hypertrophy of the pituitary gland; that is, to a hypersecretion occurring at the age of puberty or age of general or symmetrical body growth and development. He believes further that gigantism will remain such as long as the pituitary body is in normal hypertrophy, but that these cases of gigantism will assume later an acromegalic type, if, as is often the case, the pituitary body begins to take on pathological conditions. In other words, he believes that an excess of normal secretion from the pituitary gland is the cause of gigantism, while perverted secretion is the cause of acromegaly. This conception is very different from that of Brissaud and Meige, in that it attributes the lesions, which we call gigantism and acromegaly, to two distinct and separate states of the pituitary function. Brissaud and Meige's view implies that the same condition of the pituitary function is at work in both cases, any differences in the results produced being attributable to the age period at which the process begins. We know so little of the nature of the normal function of the pituitary body, and indeed of its disturbances, that it would be hazardous as yet to express an opinion either way. For my part I cannot understand the term "normal hypertrophy," as applied to the pituitary. We have, it is true, what might be called normal or physiological hypertrophy in the case of the pregnant uterus and possibly in the functioning breast, yet this is but a temporary condition and is paralled, so far as I know, nowhere else in the body. Gigantism is an abnormal condition, and to my mind cannot be explained on the basis of a "normal" hypertrophy. It may, however, be true that it is due to an excess of pituitary secretion. But if this can produce increase in the length of bone, why is it not also competent to produce increase in thickness of bone? One seems as likely as the other. Whether acromegaly is due to a hypersecretion on the part of the pituitary, as many seem to think, or to a diminution of the secretion, or again to a perverted secretion, cannot, however, be regarded as settled. Tumors, cysts, and plain hypertrophy of the pituitary have been found in the majority of autopsies on acromegalic cases, and tumors of the pituitary in acromegalic giants (Buday u. Jancto,[36] Oestreich u. Slawyk[37]). Possibly simple hypertrophy or adenomatous growths may imply oversecretion; but cysts or destructive tumors, like the sarcomata that are so frequently found, might be interpreted as lessening the amount of secretion. Conversely, tumors of the pituitary may exist without signs of acromegaly, as in two cases that have come under my own observation. Both were malignant (one sarcoma and one endothelioma). Here we must assume either that the pituitary was able to furnish the proper amount and kind of secretion, or else that compensation had taken place. We are realizing more and more the importance of the principle of compensation in regard to the body metabolism. We see, for instance, that there is a close relationship between the thyroid gland and the pituitary body. In acromegaly the thyroid gland has been found hypertrophied, cystic, or atrophic, and the disease may be complicated by the symptoms of exophthalmic goitre or myxœdema. In this connection may be mentioned a most remarkable case, reported by Pope and Clarke,[38] in which a man suffering from acromegaly had a daughter with myxœdema and an atrophied thyroid, who at the age of twenty presented the physical and mental characters of a child of five. Ponfick, Hymanson, Pineles, and Green, in particular, have noted the association of acromegaly with myxœdema, and Murray[39] its combination with exophthalmic goitre. Conversely, the pituitary has been found enlarged in cases in which the thyroid was atrophied (Boyce and Beadles[40]), and when this occurs it seems to prevent at least the immediate results of thyroid defect, namely, cretinism or myxœdema. In the article on *Dwarfism*, by the present writer, in this volume, the relationship of thyroid dystrophy to that other anomaly of growth allied to gigantism, namely, dwarfism, is dealt with at length, and it is there shown how the condition of athyroidea may result in inhibited growth and genital insufficiency. The stigmata of infantilism in acromegaly and in gigantism have suggested the possibility of disorder of the thyroid in these affections, and there have not been wanting those who would attribute acromegaly to thyroid dystrophy. Facts, however, do not favor this view.

Genital hypoplasia and malformation, as well as genital inadequacy, have been met with in dwarfism, cretinism, infantilism, gigantism, and acromegaly, and this leads us to discuss in how far disorders of the sexual apparatus are responsible for anomalies of growth. In this connection a number of interesting facts may be adduced. The sexual languor, as it might be termed, found in both acromegaly, and gigantism, has been referred to. Garnier and Santenoise[41] have observed a case of gigantism associated with feminism, cryptorchidism, and polysarcia. Thoma[42] mentions having met with defective formation of the genital organs in a case of hemihypertrophy. In acromegaly, as soon as the changes in the bones become manifest, the secondary sexual attributes are changed. In the male the hair becomes scanty, while in the female hair is apt to grow on the face much as it does after the menopause or in ovarian disorders. The larynx hypertrophies and the voice deepens. Infantilism and hypoplasia of the genital organs have also been observed in cases of tumor growth in the pituitary in the absence of signs of acromegaly. Some years ago I performed an autopsy on a woman about thirty years of age who had a perithelial sarcoma of the pituitary without signs of acromegaly, in whom the genital organs were markedly undeveloped. Babinski also reported to the Neurological Society of Paris (June 7th, 1900) the case of a girl of seventeen, who presented the signs of infantilism, amenorrhœa, abundant fat, scantiness of hair, but without acromegaly. She developed pains in the head with disordered vision, and epileptiform convulsions. After

death it was discovered that she had a tumor of the pituitary. It is clear then that there is some relationship between lesions of the pituitary and thyroid glands and genital disturbances. What, then, is the primary disorder which leads to such extraordinary anomalies of growth and development? Breton and Michaut[43] have suggested that there is a trophic deviation of the genital activity to the bone marrow so that the medullary bone-forming function preserves its activity indefinitely. The cessation of genital activity would lead to acromegaly. This view is somewhat similar to that promulgated previously by Freund, Klebs, and Verstraeten, who held that there is a disturbance of the evolution of the genital function. If genital evolution is in excess we get gigantism and acromegaly; if defective, we get infantilism and dwarf growth. It is, of course, well recognized that with the onset of puberty the efflorescence of the sexual characteristics is coincident with increased growth and development of the body as a whole. The operation of castration has been observed to exert a notable effect on the stature of the body as well as in inhibiting the development of the secondary sexual peculiarities. In eunuchs the height is often extreme. This is due chiefly to a disproportionate increase in the length of the legs. Lortet has confirmed this statement by an examination of the skeleton of an Egyptian eunuch 196 cm. high. In castrated animals, the capon and the ox, the same increased growth of the lower or hind extremities is to be observed. Silva[44] has further recorded a curious observation in a youth who was normal until the age of thirteen. The testes then remained atrophic and when about twenty he began to grow rapidly, eventually manifesting some enlargement of the head and extremities, muscular weakness, anosmia, slight scoliosis, to such a degree as to suggest acromegaly.

While such facts as those just mentioned are suggestive of some relationship between genital insufficiency and disorders of growth and nutrition, to my mind the evidence is not strong enough to induce us to accept the view that deficiency of the genital organs is the cause of these disorders. Two-thirds of the cases of acromegaly develop after puberty is practically reached. The loss of sexual power in the male is gradual and progresses *pari passu* with the extension of the disease itself. In the female, too, while amenorrhœa is a frequent and often the first symptom of the disease, it is not invariable. Again genital hypoplasia and other signs of infantilism are often present in dwarfs, and the argument might be applied with equal force to explain dwarfism. The same cause could hardly produce at one time dwarfism and at another gigantism. Moreover, while genital hypoplasia has been often observed in cases of thyroid atrophy and gross lesions of the pituitary body, so far as is known castration does not produce a converse effect on these particular organs. While, then, genital hypoplasia undoubtedly plays some rôle in osteogenesis, it seems to be quite a subordinate one, and appears to be inadequate to explain the more marked aberrations from the normal path of development. The functions of the thyroid gland, the pituitary body, and the sexual organs are, however, no doubt correlated, and it is probable that the normal course of growth and development is dependent on a certain balance of power exerted by these glands. Of what nature is this correlation we are to a great extent in the dark. It is generally believed that the glands mentioned produce internal secretions that are essential to the normal course of the metabolic processes. The evidence in favor of this is less strong in the case of the sexual organs (testes and ovaries) than for the other organs. It may be inferred that while the metabolic processes referred to are vital in nature, they are inextricably associated with chemical transformations. The importance of chemical substances in the growth of the organism is well illustrated by the experimental work of Wegner, Maas, and Gies.[45], [46], [47] Wegner proved that by feeding rabbits with minute doses of phosphorus for a prolonged period he could get a marked increase in the formation of bone at the epiphyseal sutures of the long bones. The same thing has been found to occur with arsenic. Observations upon the nature of the metabolism in giants are hitherto lacking, but we have considerable evidence to show that in acromegaly metabolism is disordered. There appears to be a tendency to an overproduction of lime salts in acromegaly. Deposits of lime have been found in various parts of the body, especially in the pituitary, the thyroid, and the vessels (arteriosclerosis). Ossiform infiltration of the dura mater has been observed. Von Moraczewski[48] has also demonstrated a tendency to the retention of lime and phosphorus in the system in cases of acromegaly. Not only then is there an increased deposit of lime at the extremities of the bones, but also in widely distant parts of the body.

We are, I think, led to the inevitable conclusion that gigantism, like acromegaly, is very often a disorder of development brought about by abnormal metabolic processes. We must also admit that a large proportion of cases of gigantism are etiologically the same thing as acromegaly, and that an additional but uncertain number are probably abortive acromegaly (acromégalie fruste). One consideration must, however, be by no means overlooked in any discussion of the question of internal secretion. The doctrine of internal secretion as at present understood implies the existence of certain substances in the body upon which the secretion of the glands in question may act. Now the gland, thyroid or hypophysis, may be totally unable to perform the duties required of it, owing to some lesion, or it may be only relatively so. In either case similar symptoms would arise. This doctrine of relative inadequacy has been advanced by Prof. J. G. Adami,[49] and has by no means attracted the attention it deserves. On the one hand, relative inadequacy of a gland will set in as soon as its reserve power has been exhausted, and may increase until it becomes absolute. On the other hand, there may be an excess of the substances upon which the internal secretion is supposed to act. Therefore it is quite possible that certain forms of developmental disorder may be due to relative inadequacy on the part of some of the important glands, that, as we have seen, are competent to modify nutritive processes. In the case of gigantism, relative inadequacy of the pituitary, or it may be a relative overadequacy, short of producing the regular symptoms of acromegaly, might influence growth so as to bring about excess.

However this may be, and the deduction is alluring, there still remains some small proportion of cases of gigantism which cannot be explained on any of these theories. Such are the cases in which in addition to excessive height there is great strength with perfect proportion. Here there can be no question of disease in the ordinary acceptation of the term. Such giants are examples of the so-called "athletic" habit of body, and are strictly comparable to the giant infants before referred to. They represent the structure of the human body carried to its highest point. They may be regarded as examples of *true* or *essential* gigantism. Infantilism and pituitary dyscrasia cannot explain them. Rather are they to be referred to peculiarities inherent in the germinal cells of the progenitors. This view is supported by the fact that certain anomalies, for example polydactyly, malformations of the genital organs, and congenital hydrocele, are apt to be associated with the increase in size and weight. *Albert George Nicholls.*

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HÆMOLYSIS.—(Synonyms: Hæmocytolysis; Hæmatolysis; Laking of blood; Globulysis; Erythrocytolysis.)

Although etymologically this term includes destruction or solution of both red and white corpuscles, yet by usage it has come to be applied, when used without specification, only to the erythrocytes. When corresponding changes of the leucocytes are considered, the specific term *leucolysis* or *leucocytolysis* is generally used. In this article the term hæmolysis will be used, as above indicated, to apply only to *erythrolysis*.

In hæmolysis the essential phenomenon consists in the escape of the hæmoglobin from the stroma of the corpuscles into the surrounding fluid. As it is not exactly known in what way the stroma holds the hæmoglobin normally, whether purely physically or in part chemically, or whether the stroma consists of a spongioplasm or a sac-like membrane, or both, the ultimate processes that permit the escape of the hæmoglobin are not finally solved. However, the agents by which the escape is brought about are well known and extensively studied, and they are found to be of extremely various natures. They may be roughly classified as: (1) Known physical and chemical agents; (2) unknown constituents of blood serum; (3) bacterial products; (4) certain vegetable poisons; (5) snake venoms.

While the known chemical and physical agencies in the production of hæmolysis have much significance in physiology, and to some extent in pathology, yet the importance of the subject of hæmolysis at the time of this writing rests chiefly upon the work now being done with blood serums; and in turn the chief importance of this work lies in its relation to problems of bacterial destruction, cell destruction, and the general laws of cell susceptibility and cell resistance. Hence we shall devote particular attention to the subject of serum hæmolysis, appreciating that whether time does or does not show this work to be of as far-reaching importance as is now hoped, yet in any event it will mark a distinct period in the history of medical science. As being by far the simpler, however, we shall first discuss:

(1) Hæmolysis by Known Chemical and Physical Agencies.

If distilled water is added to corpuscles of any kind, osmotic changes are bound to occur, since within the cells are abundant salts, soluble in water, which will begin to diffuse outward in an attempt to establish osmotic equilibrium between the corpuscles and the surrounding fluid. Conversely water enters the corpuscles at the same time, and accumulating there leads to swelling until such injury has been produced as permits the hæmoglobin to escape and enter the surrounding fluid. Before this occurred the fluid was opaque because of the obstruction to light offered by the red cells. The stroma now settles to the bottom, while the hæmoglobin diffuses into the fluid, making it red, but perfectly transparent. This process has long been known as the "laking" of blood, and is essentially the condition present in all forms of hæmolysis. That the hæmoglobin escapes only through injury of the stroma and not through simple osmotic diffusion is shown by the fact that if salt solution of the same concentration as normal serum is used instead of distilled water, no such escape of hæmoglobin occurs. As hæmoglobin is perfectly soluble in the salt solution it should pass out if it diffused as do the salts. Since there is no escape of hæmoglobin in such a salt solution, it is evident either that the stroma is not permeable to hæmoglobin, or else the hæmoglobin is in some way attached to or combined with the stroma. Again, if the corpuscles are placed in a solution of salt more concentrated than their own fluids, water escapes and the corpuscles shrink; as no hæmoglobin escapes with the water it is evident that the stroma is not permeable to hæmoglobin when intact. Therefore it would seem that hæmolysis by distilled water may be purely physical, produced by the cell stretching until rupture occurs and the hæmoglobin escapes as from a sac, or else it may be that the stroma is partly soluble in water but not in salt solution, so that the distilled water dissolves the stroma and the hæmoglobin escapes from its attachment. Because of the resemblance of the process of hæmolysis to the rupture of plant cells with escape of their contents when they are placed in distilled water, it might be assumed that hæmolysis is largely a physical matter, but there are many indications that chemical changes must be involved. For example, if a red corpuscle in an isotonic solution is cut into pieces the hæmoglobin does not escape, indicating that its structure is quite dissimilar to that of the simple vegetable cell, and that there is some union of stroma and of hæmoglobin other than physical.

Repeated alternate freezing and thawing is another physical means of bringing on hæmolysis. Heating to 62°–64° C. causes hæmolysis of mammalian corpuscles; in cold-blooded animals this seems to occur at a slightly lower temperature.

Some chemical agents, as might be expected, are capable of liberating hæmoglobin, even when the corpuscles are in isotonic solutions. The ordinary salts of serum, of course, do not have this property, but ammonium salts are strongly hæmolytic. Urea also will dissolve red corpuscles. The chemical agents that dissolve red corpuscles seem to be those that have the power of penetrating the stroma. Ammonium salts and urea penetrate the corpuscles freely and cause hæmolysis. Sugar and NaCl seem not to penetrate the corpuscle, and therefore do not produce hæmolysis. Of the permeating substances there seem to be two types: One, like urea, does not produce hæmolysis when in a solution of NaCl isotonic with the serum; the other, like ammonium chloride, is not prevented from producing hæmolysis by the presence of NaCl. All these agents seem to effect hæmolysis by acting on the stroma, for when the stroma of corpuscles

hardened in formalin has its lecithin and cholesterin removed with ether, saponin, a powerful hæmolytic substance, seems to have no effect. The action of saponin and of many other hæmolytic agents can be prevented by the presence of cholesterin in excess, suggesting that it is this constituent of the stroma that is affected. The fact that chloroform, ether, and amyl alcohol will cause laking is probably intimately connected with the fact that lecithin and cholesterin, important constituents of the stroma, are both soluble in these substances. Arseniuretted hydrogen when inhaled causes intravascular hæmolysis, and there are many other drugs and chemicals with the same property, among which may be mentioned nitrobenzol, nitroglycerin, and the nitrites, guaiacol, pyrogallol, acetanilid, and numerous aniline compounds. The bile acids and their salts will also produce hæmolysis, as seen in jaundice. Sodium bicarbonate solutions of one or two per cent. are hæmolytic for some varieties of corpuscles, but 0.1 per cent. Na_2CO_3 and $NaHCO_3$ do not cause hæmolysis.

Leucocytes are dissolved by some of these agents, particularly the bile salts, although they are affected by no means so rapidly or so much as are the erythrocytes. There seems to be no relation between the erythrolytic and leucolytic powers of these substances. Water causes swelling, with solution of the granules in time, and the same is true of ammonium-chloride solutions.

(2) Hæmolysis by Serums.

With these facts as to the physical and chemical properties of the red corpuscles, we may consider the features of serum hæmolysis. Since a very early time it has been known that it is not possible to substitute the blood of animals for the blood of man by transfusion, because the corpuscles of both transfused and native blood soon suffer destruction. Animal experiments also showed that as a general rule the blood of one animal cannot be substituted for that of another of a different species. This observation was not extended, however, until attention was drawn to it later by experimental investigations that may be said to have begun with the observations of Belfanti and Carbone. They found that if the red corpuscles of a rabbit were injected into a horse repeatedly, the serum of the horse became very toxic for rabbits, because it caused dissolution of their red corpuscles. It also developed that this same hæmolytic property was manifested when the serum was added to rabbit corpuscles in a test tube. When Bordet showed the similarity of this process with the solution of bacteria by serum, a process that had already been studied in a similar manner, the phenomenon of hæmolysis by serum suddenly leaped into importance, and has now for some time occupied the attention of a large part of the bacteriologic and pathologic laboratories of the world. In hæmolytic experiments we have a means of studying the property of blood serum of destroying cells under varying conditions, which is extremely easy to observe and control as compared with the less readily examined bacteria or tissue cells. Whatever the future may develop as to their ultimate worth, there can be no doubt that hæmolysis experiments have given us many new and clear conceptions of the means of defence of the body against bacteria, and also of changes in cells of other sorts, that would not have been secured by any other method.

The manner of conducting hæmolysis experiments is usually about as follows: Blood corpuscles of the kind to be tested are secured by defibrinating the freshly drawn blood in the usual way, by whipping. A five-per-cent. solution of these corpuscles is made by adding 19 parts of 0.75 per-cent. NaCl solution, which is isotonic with them. This emulsion is placed in test tubes, very small ones by choice in order to save material, and the serum that is to be studied is added to it. It is necessary that the tubes be cleaned as for chemical research and sterilized, and all steps of the experiments should be under aseptic precautions to prevent bacterial action affecting the experiments. As Jordan has shown that even the degree of alkalinity possessed by some varieties of glassware when new may cause hæmolysis, the tubes should be cleaned with the usual acid-cleaning fluid. The tubes, stoppered with cotton, are kept at 37° C., and in the course of from fifteen minutes to two hours the hæmolysis will be manifested by the diffusion of the hæmoglobin upward into the supernatant fluid, while the turbidity produced by the red corpuscles disappears. At the bottom of the test tube the stroma collects as a slight sediment.

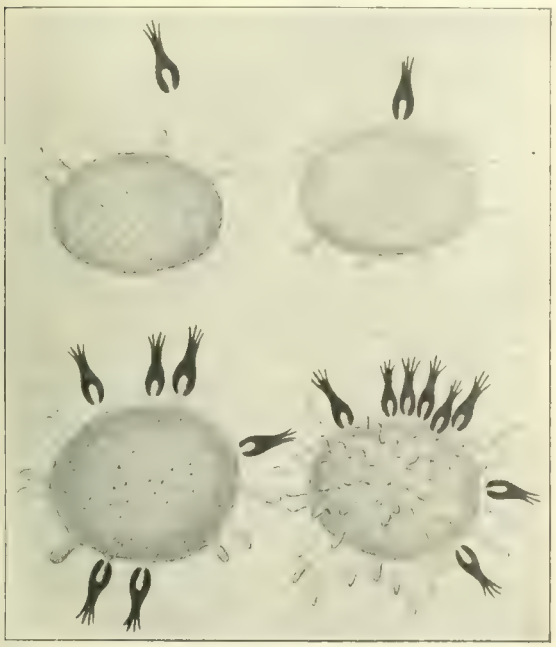
The Mechanism of Hæmolysis.—If a serum from an animal immunized against the red corpuscles of another animal is allowed to act upon such red corpuscles in a test tube, hæmolysis occurs promptly. Bordet showed that this property was lost if the serum was heated half an hour at 55 C., indicating that the destroying agent was very sensitive to heat. In addition he found that if to such heated serum, deprived of all hæmolytic power, there was added a small amount of serum from an animal that had not been immunized and which was of itself inert, the combination was quite as active as the unheated immune serum. In other words, there is contained in normal serum a substance easily destroyed by heat, that needs to be present to cause such specific hæmolysis. But this *thermolabile* substance alone is not able to dissolve the red corpuscles, as the normal serum is found to be quite inactive; it is necessary also to have present some second substance that appears in the serum during the process of immunization. And as heated serum is also quite inactive it is apparent that this heat-resisting (*thermostable*) substance is not of itself able to dissolve the corpuscles. Therefore evidently two substances are needed to dissolve the corpuscles: one, which is easily destroyed by heat and which is present in normal serum; the other, which is present in sera of immunized animals, and which resists heat. Before Bordet had demonstrated these facts about the red corpuscles he had found out that the same conditions prevailed in the destruction of cholera spirilla by the serum of animals immunized against them—two similarly behaving bodies are required in the solution of the organisms, the so-called "Pfeiffer's reaction." Out of these fundamental observations have grown the vast amount of research on serums in their relation to immunity, and on them have been based the theory of Ehrlich as to the ultimate nature of the processes of bacterial and cellular destruction that protect the body from infection and disease, and which perhaps play a part even in normal metabolism.

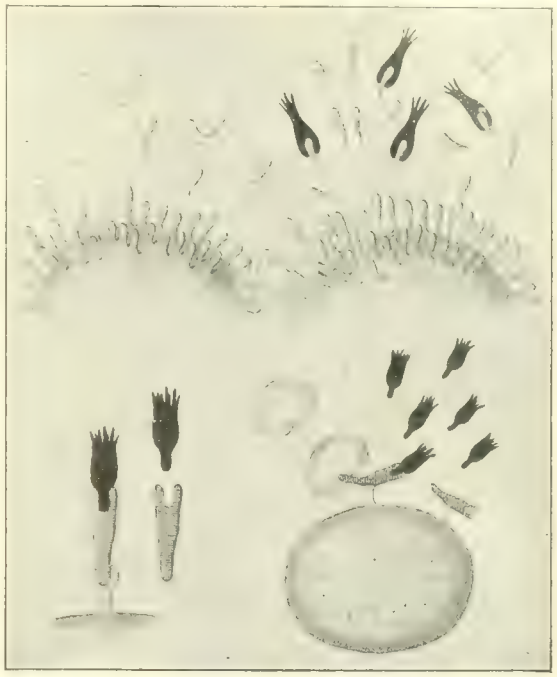
Ehrlich's Theory of Hæmolytic Processes.—Although at this time Ehrlich's ideas stand only as theories, and nothing more, still the fact that they have given us some sort of mental image upon which to base investigations of undoubted value, places them in a certain position of permanence. For this reason we shall endeavor to set them forth briefly in this article.

The Nature of Toxin and Antitoxin.—The fundamental feature of Ehrlich's theory rests upon a conception of the manner in which a toxin attacks a cell. If we consider a cell purely as a mass of various chemicals, and a toxic material as another chemical substance, either simple or complex, it will be apparent that the toxic substance will affect the cell if there is a chemical affinity between them. If there is no such affinity that particular toxic substance is not harmful for that particular cell. On the other hand, if the toxic substance and the cell do possess a chemical affinity they will unite, and the composition of the cell will be altered. When the uniting substance is toxic the result of the union is an injury of some kind to the cell. Undoubtedly other substances may unite with the cell without injuring it, for example, food supplies.

If this line of reasoning be carried still further, it will be readily seen that of the many substances of different chemical nature that compose a cell, not all can have the same degree of affinity for the toxin. By ordinary chemical laws the substance that has the greatest affinity will attract the toxin until it is saturated, and only on condition that there are other substances with affinity of varying degrees will more than the one susceptible substance unite with the toxin. We can thus conceive of

a cell with one or more constituents that may become united to any given toxin with varying readiness. To these cell components that combine with the toxin the name *receptor* has been given by Ehrlich, and is generally applied. It will be readily seen that if a cell is affected by a toxin that fact implies the presence in the cell of a receptor for the toxin. Conversely an absence of proper receptors will explain the lack of susceptibility of certain other cells to the same toxin. For example, we may consider that some animals are immune to tetanus because the cells of their nervous systems contain no receptors that will combine with the tetanus toxin. To make the analogy to chemical reactions, Ehrlich has likened the receptors to the various *side chains* of organic compounds.





FIGS. 5153 and 5154. Ehrlich's Diagrams Illustrating the Mechanism of Immunity and Cytolysis. 1, 2, and 3 illustrate different forms of receptors, showing the necessity for agreement of the combining bodies. The figures in black indicate substances with toxic action. 4, 5, and 6 illustrate the excessive production of receptors in response to the action of toxins, and their escape from the cell; in 6 they are seen to combine with toxin outside the cell, preventing its union with the cell; 7 shows the structure of the complement and intermediary body of bacteriolytic and cytolytic sera; 8 shows the amboceptor, while attached to the cell, uniting the complement to a large molecule.

Figs. 5153 to 5157 represent in diagrammatic form the principles involved, in which definite forms are made to indicate chemical groups, and differences in their configuration to indicate differences in chemical affinity. The protrusions from the cells indicate the receptors or "side chains" that combine with outside substances. Each particular variety of receptor combines with the particular toxin for which it has a chemical affinity, as indicated by correspondence of configuration. In these diagrams toxic bodies are always indicated in black; and the black objects represent toxins which combine with the particular receptors they fit, or, in other words, for which they have a chemical affinity.

The body known as antitoxin is evidently one that has the power of combining with the toxin, for it has been demonstrated repeatedly that mixtures of toxin and antitoxin in proper proportion that have stood together a short time are quite inert; the union seems to be after the nature of the union of chemicals. This fact likens antitoxin to the receptors which have just been described, and in fact it is considered that antitoxin and receptor are identical substances, with the difference that the receptor is a part of a cell, while the antitoxin exists free in the serum. Ehrlich's explanation of the formation of antitoxin is as follows: When the toxin combines with the receptors of a cell, the cell is deprived of these receptors for whatever use they may have under normal conditions. Obeying the laws of regeneration the cell replaces these lost groups by new ones; indeed it replaces them in excess, much as in the healing of a wound there is an excessive formation of new cells. The excessive receptor bodies fall away from the cell into the serum, where, if they meet with any toxin, they will combine with it just as well as if they were still attached to the cell. Of course if the toxin is saturated with receptors while in the serum, it is devoid of any affinity for the receptors attached to the cells and does not harm the cells. In this way the cells are protected from the toxin. So, when we inject diphtheria antitoxin into the body of a patient, we are merely introducing receptors from the susceptible cells of a horse. These meet with the molecules of diphtheria toxin while it is still in the blood, and combining with it there prevent it attaching itself to any of the cells of the patient, and so it is rendered incapable of causing harm. The diphtheria antitoxin is not only able to combine with diphtheria toxin which is in the circulation, but if in excess to wrest from the cells toxin which may have already been combined, probably by the law of mass action. This always happens when a case of diphtheria is cured by

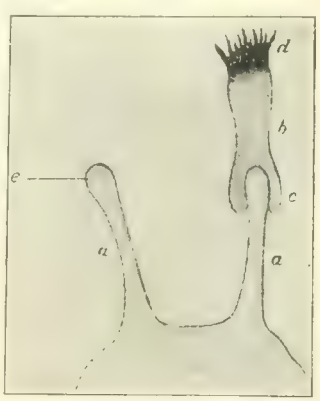


FIG. 5155.—Receptor of the First Order [illegible]. Haptophore complex; *b*, combined toxin molecule, with haptophore and toxophore groups. (After Ehrlich.)

antitoxin, and the clinical evidence of the "wresting" process is the sudden subsidence of the disease. It is not so easy to wrest tetanus toxin from the nervous tissue with antitoxin, and accordingly tetanus is not often cured by antitoxin.

One of the strongest proofs of Ehrlich's conception of antitoxin and toxin is that furnished by Wassermann's experiment. This consists in permitting tetanus toxin to stand for some time in contact with nervous tissue; it will then be found that the fluid part has lost all of its toxic property, and further, that the cellular portion which presumably contains the toxin is also not toxic. This agrees fully with Ehrlich's idea that a toxin attacks the cells that have receptors for it, and when so combined is harmless for other cells. In this case the nerve cells have combined with the toxin just as does antitoxin and have rendered it unable to attack other nerve cells. Other tissues are found to be quite unable to fix tetanus toxin in this way. A similar action has been found by Flexner to exist between nervous tissue and the specific nervous poison of cobra venom. The union of toxin and antitoxin seems to be of strictly chemical nature, for it follows the usual laws of chemical union, and it seems impossible to separate again the toxin and antitoxin after they have combined.

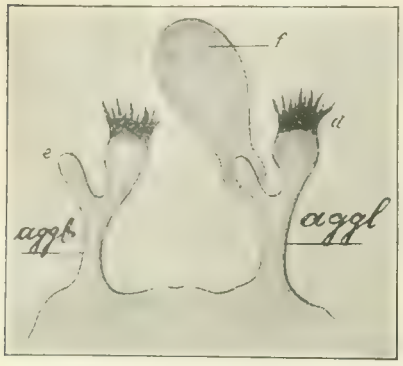


FIG. 5156. — Receptor of the Second Order (*aggb*, with haptophore (*e*) and zymophore (*d*) groups; *f*, combined food molecule. (After Ehrlich.)

No. 4, of Fig. 5153, and No. 5, of Fig. 5154, illustrate the overproduction of receptor groups, which are liberated and enter the blood plasma. No. 6 (Fig. 5154) indicates the combining of the receptors with the toxin molecules, and shows how incapable they now are of combining with the cell.

In the process of immunization, under this conception, the receptors of the cells are repeatedly combined with toxin, and the resulting reaction on the part of the cells causes the discharge of large numbers of free cell receptors into the blood. These receptors give the serum whatever antitoxic property it may have.

The Structure of Toxins.—We have referred to the fundamental conception of a toxic substance as a substance which by combining with the receptor of a cell injures the cell in some way. It has been developed that toxin accomplishes this injury by a portion of itself that is different from the portion that combines with the receptor. In other words, a toxin consists of a substance that binds it to the cell, and of another that causes the injury to the cell. This may be explained best by describing the facts that gave rise to this idea. When a toxin, say tetanus toxin, has been kept for some time, it is found that its toxic action decreases until relatively very large amounts are required to produce symptoms of tetanus in animals. Such a weakened toxin, however, requires just as much antitoxin to neutralize its toxic action as it did while possessed of its full strength. As the antitoxin is merely an accumulation of free receptors, it seems that the toxin during the process of weakening has lost none of its power to unite with receptors, but rather has lost its power to cause injury to the cell. The group that attaches itself to the cell receptor has been called by Ehrlich the *haptophore* group, while the group that injures the cell is called the *toxophore* group. Toxins that have become weakened while still retaining their power to combine with antitoxin are referred to as *toxoids*, and are supposed to be toxins that have lost the toxophore group but have retained the haptophore group. In the diagrams of Ehrlich the fringed portion of the toxin figure represents the toxophore portion; the part fitting with the receptor, the haptophore.

It may be mentioned that this degeneration of toxins into toxoids has practical application in immunization, for since toxoids are just as capable of combining with cell receptors as are toxins, they can be used to produce antitoxin without danger of causing intoxication.

The Relation of Toxins to Hæmolysins.—While the above discussion of the nature of toxin and antitoxin does not directly apply to the subject of hæmolysis, yet it is necessary to an understanding of the principles of cytolytic phenomena, since out of this conception of the nature of immunity against toxin has come our present conception of the nature of immunity against cells. Animals are immunized against foreign blood corpuscles just as they are against bacteria and against toxins, by repeated injections of small amounts of the foreign substance. Similarly in each case their serum comes to contain a substance capable of protecting the animal against the injected material. However, there is one important difference between immunity against toxin and immunity against cells, whether these cells are bacteria, blood or tissue cells matters not. To neutralize a toxin it is merely necessary to occupy the group of the toxin that unites with the cell receptors, for then the toxin cannot unite with the cells to injure them; in this harmless condition the toxin is destroyed or eliminated. In the case of the cells, however, it is necessary that they be destroyed by the serum, and this requires more than the entrance into them of some body from the serum; they must be attacked somewhat in the way a toxin attacks a cell. In fact, a serum immunized against a cell is really a toxin for that cell, and like the bacterial toxins it possesses two groups, one combining with the cell, and the other that attacks the cell. However, there are certain important differences between bacterial toxins and immune serums. It will be remembered that it was found that both bacteriolytic and hæmolytic serums lost the power of producing their specific effects of cell destruction when heated for half an hour at 55° C., and that they regained this power in full when to them was added some normal serum, which alone was quite inactive. From this it was deduced that two substances enter into the cytolysis: one susceptible to heat and present in normal serum, the other more resistant to heat, and present only in immunized animals. Comparing the cytolytic serum with the toxin we see that the chief difference lies in the fact that one of the cytolytic bodies is present normally in the serum, and can be supplied quite readily to make the other body active. In its susceptibility to injurious agents and in its power to

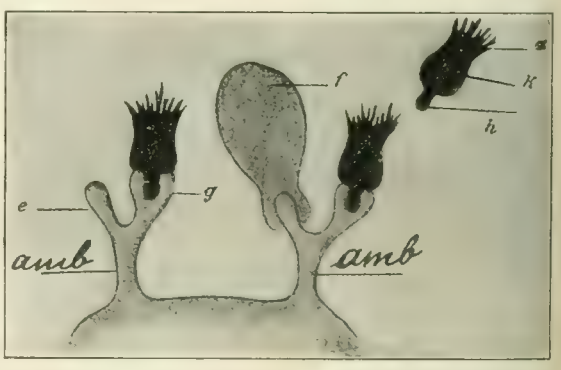


FIG. 5157. Receptor of the Third Order. *amb*, The receptor; *e*, haptophore (cytophile) group; *g*, complementophile group; *K*, complement, with haptophore (*ho*) and zymotoxic (*z*) groups; *f*, combined food molecule. (After Ehrlich.)

destroy cells this thermolabile substance resembles the toxophore group of the toxin. As it has to be added to the body that is developed during immunization to render the latter active, it has been given the name of *complement*, indicating that it is a complementary substance in the reaction. Another name sometimes applied to the same body, *addiment*, is of similar significance. On the other hand, the body developed in the serum through the process of immunization, is quite like the haptophore group of the toxin, in that it is more resistant to injurious influences, and, as will be shown later, is concerned in uniting the complement to the cell to be attacked. As it has two affinities, one for the cell, the other for the complement, it has been called by Ehrlich *amboceptor*, implying the double affinity. A receptor, for example, having but one affinity may be called a *uniceptor*. Another name commonly given to the amboceptor is *immune body*, because it is the specific substance that confers immunity; but, as this or a similar body may be naturally present in the serum of animals that have not been immunized, this name can be used only for specifically immunized animal serum, and the more general term, *intermediary body*, is used except in specific instances.

The Mechanism of Hæmolysis.—Our understanding of the phenomena of hemolysis is therefore as follows: During immunization the immune bodies are developed, which have the property of combining with the red cells, attaching themselves to the receptors of the corpuscles. They combine on the other side with the complement that is present normally in the serum, even before immunization, and by so attaching it to the corpuscles enable it to exert its destructive action. This arrangement is indicated by No. 7 (Fig. 5154), in which the black fringed body represents the complement, united by the amboceptor to the red cell receptor. Beside it are shown free the two constituents of the hæmolysin. Without being attached in this way the complement is quite inert. That the immune body is attached to the corpuscles is shown by the following experiment: If an immune serum is heated the complement is destroyed, and we have the immune body in an inactive condition in the serum. This inactive serum is mixed with red corpuscles, and kept for fifteen minutes at 45° C.; the red corpuscles are then separated by centrifugalization. The supernatant fluid is removed and added to other red cells. If it still contains intermediary body it should be able to dissolve the corpuscles when fresh normal serum, containing complement, is added. As no hæmolysis does occur it appears that all the intermediary body has been taken out of the serum by the red corpuscles. That this is the case can be proved by adding to these corpuscles some normal serum which contains complement, but no intermediary body, for the corpuscles are now quickly dissolved. Therefore all the intermediary body must have been united to the red corpuscles during the fifteen minutes' exposure at 45° C. Another demonstration of this is made as follows: If just enough red corpuscles, heated immune serum, and fresh normal serum are mixed at 0° C. in the proportions required to saturate all the affinities and to leave nothing over, on removing the corpuscles it will be found that all the complement is in the supernatant fluid, and all the intermediary body is attached to the corpuscles. This indicates that the affinity of the intermediary body for the receptor of the corpuscle is greater than its affinity for the complement, and also shows that at 0° C. the complement and intermediary body can exist side by side without combining.

The foregoing are the fundamental facts concerning the mechanism of hæmolysis, and the facts themselves are generally accepted. However, there are those who oppose the theory advanced by Ehrlich in explanation, contesting it on various grounds. For instance, by some it has been thought that the intermediary body acts after the manner of a mordant, simply modifying the cell so that it absorbs the complement, and all the features of hæmolysis are considered manifestations of physical rather than of chemical action. Nevertheless, at the time of writing it has been possible to fit all the facts that have been developed into accord with the theory, and there is no question that the theory has been of immense value in giving a ground from which to proceed in new investigations of the laws and processes of immunity. In defending the theory, however, it has been found necessary greatly to amplify and modify the original simple conception stated in the preceding paragraphs; and, as this process is still going on, it will be impossible here to give a complete account of all the changes so made. Considering each by itself, we shall make an attempt to give the chief facts concerning the two agents in the hæmolytic process.

The Intermediary Body.—This factor in the cytolytic process has had an unfortunately large number of names applied to it, leading to much unnecessary confusion. Immune body and amboceptor have already been mentioned and explained. French writers often use the term, *substance sensibilisatrice*, with the view that its action is to prepare the corpuscle for the action of the complement. Rarely used now are the terms *fixator*, *desmon*, and *copula*. In general the name "intermediary body" (German, *Zwischenkörper*) is to be preferred, unless we are dealing with a specific substance obtained by immunization, when the term "immune body" may be used.

Its exact nature is totally unknown, for it has not been found possible to isolate it from other constituents of either serum or blood corpuscles. The fact that it is generally deprived of its action at about 70° C. would suggest that it is either a form of proteid or is combined with one. However, thermolabile intermediary bodies have been described; like the complement they are destroyed at a lower temperature. The intermediary body does not seem to develop an affinity for the complement until it has first combined with the cell.

In immunization the body is formed in large quantities, much as is the antitoxin. As a rule the greater the difference in the nature of the animals used the greater the activity of the resulting serum. Rapid absorption of large quantities of corpuscles is also desirable, to which end the blood is usually diluted with an equal quantity of 0.75-per-cent. salt solution and injected intraperitoneally. Ehrlich explains the formation of the immune body on the same basis as the antitoxin formation is explained. In its ordinary processes of nourishment each cell must combine with proteid molecules so large that in comparison with them the toxin molecules are small indeed. Such giant molecules cannot be used by the cell as they are, but are made available by means of a ferment-like process which splits them up into smaller fragments. This act is pictured as being accomplished by a group attached to the cell, which has one arm with affinity for the proteid molecule and another for the ferment (see No. 8, Fig. 5154). In this way the proteid molecule and the ferment are united in order that the proteid may be acted upon. It will be seen that this is merely an amplification of the idea of the toxophore group of the toxin, which is attached to the cell by the haptophore group, in order that it may produce its injurious effects. In hæmolysis the red corpuscle is considered in the place of the proteid molecule, and in immunization against red corpuscles we simply have large quantities of such "side chains" as have this double affinity for corpuscle and ferment, cast off in numbers into the plasma. These side chains, then, are the intermediary bodies, which by the nature of their affinities are able to unite the complement to the red corpuscles and to accomplish their destruction.

Normal serum may contain bodies with the same properties as the immune bodies. For example, dog serum has normally considerable hæmolytic action on guinea-pig corpuscles, and human serum on rabbit corpuscles. That this is due to the action of a true intermediary body is shown by the fact that when the serum is heated and the dog complement is destroyed, normal guinea-pig serum when added will furnish complement and hæmolysis will occur. This also indicates that one particular intermediary body may unite with more than one sort of complement, for in this instance guinea-pig complement has taken the place of dog complement, and has united

with amboceptors from dog serum. So far as we know, all varieties of animals may produce hæmolytic amboceptors. Noguchi has demonstrated their presence, both normally and after immunization, in both vertebrates and invertebrates.

It is to the immune body that the specific action of immune sera is due. This may be shown by placing both chicken and guinea-pig corpuscles in a drop of serum from a rabbit immunized against chicken corpuscles. The nucleated corpuscles of the chicken can be readily distinguished from the corpuscles of the guinea-pig, and it will be found that they undergo hæmolysis, while the guinea-pig corpuscles do not. It may also be mentioned that in this process the nuclei of the corpuscles are not dissolved, only the cytoplasm containing the hæmoglobin being noticeably affected.

On the other hand, it is possible for a serum to contain at the same time a large variety of hæmolytic amboceptors. These may be present normally, in which case the serum has the power to dissolve many varieties of corpuscles; or the same effect may be obtained by immunizing the animal with several varieties of blood at the same time. It has been shown that here we have not one amboceptor capable of uniting with all the varieties of corpuscle, but rather there is a special amboceptor for each variety. If one is removed by saturating with one sort of red corpuscle, the serum can still dissolve all the other sorts.

Another interesting feature of the immune body is that animals may be able to produce a body hæmolytic for other individuals of their own species; for example, a goat immunized against the corpuscles of another goat may have its serum become hæmolytic for the corpuscles of that particular goat. Such a lysin is called *isolysin*, as contrasted with the *heterolysins* formed when animals of different species are used. Of great importance is the fact that an *autolysin*, that is, a body causing hæmolysis of the corpuscles of the animal providing the serum, has not been obtained, although many experiments have been made to this end. It can be readily understood what serious results would promptly arise if such autolytic bodies were formed, and it has naturally been suggested that such a condition may exist in certain instances of auto-intoxication. In various diseases, moreover, Eisenberg found that *isoagglutinins* were present in very variable quantities, yet there were no instances in which the individual's serum was hæmolytic for his own blood. It must be admitted that at present the reason for the absence of autolysins is not satisfactorily explained.

The time required for the development of immune bodies varies greatly, as also does the time of persistence after immunizing injections are stopped. In some instances hæmolysins may be found as soon as a day after injection of corpuscles for the first time, and they are usually present in a week. In certain experiments of Ehrlich the time when maximum activity of the serum was reached varied from seven to fifteen days.

Bordet and other French observers have claimed that the union between amboceptor and corpuscle is not chemical but purely physical, but this contention seems to have been quite completely answered by Ehrlich and his followers. Ehrlich illustrates the resemblance of the reactions of intermediary bodies to known chemical substances by a comparison with diazo-benzaldehyde. By means of the diazo group the benzene radical may be united to one set of substances, such as phenols, aromatic amines, etc., while by the aldehyde group a different set of substances can be combined, including ammonia radicals and HCN. Thus by having the diazo-benzaldehyde as an intermediary body phenol and HCN can be united, the phenol in this case assuming the place of the red corpuscle, and the HCN the place of the complement. In any event it seems certain that the union of the immune body is with the stroma alone, and as physical means have been found inadequate to cause the liberation of the hæmoglobin it is apparent that some chemical change results.

Of the two combining portions of the amboceptor, the one that has an affinity for the complement is referred to as the *complementophile* group, while the one that unites with the cell is called the *cytophile;* or, in the case of hæmolysis, as the *hæmophile* or *hæmotrophic* group. It seems probable that there are also intermediary bodies that have several combining groups, and are therefore not amboceptors, but triceptors, quadriceptors, etc.

By those who consider phagocytosis of particular importance in all processes of immunity, the observations of Savtchenko, that the immune body causes the phagocytes to engulf corpuscles with great readiness, is esteemed of much significance. This increased phagocytosis is manifested by leucocytes either in the body or in the test tube, and may explain, at least in part, the increased phagocytosis observed in many diseases. Whether the phagocytosis is increased because of alterations in the red cells, rendering them more chemotactic than normal, or to direct stimulation of the phagocytes, is unknown. The former seems more probable.

Immune bodies are capable of transmission from mother to fœtus, although there is no transmission from the male parent. A rabbit immunized before or during pregnancy to certain corpuscles may give birth to young possessing similar immune bodies, and it is possible for immune bodies to be transmitted by the milk. Normally existing hæmolytic and agglutinating properties may be transmitted from mother to fœtus, but they do not necessarily agree in proportion in the blood of each; they are usually less in the fœtus.

Complement.—Because of its property of causing solution phenomena in cells, whether corpuscles or other kinds, complement is generally considered as of the nature of a ferment, and this is supported by its susceptibility to heat, which is much the same as that of the known proteolytic enzymes. Many chemical agents, such as ten-per-cent. HCl, also destroy complement. Furthermore Delezenne has shown that the union of trypsinogen and enterokinase in the intestine, that results in the production of the active proteolytic ferment trypsin, is of exactly similar nature to the union of complement and immune body. On the other hand, after hæmolysis of red corpuscles no bodies are found that agree with those produced by either tryptic or peptic digestion, and the stroma is not ordinarily dissolved, but is deposited at the bottom of the test tube as a sediment, still retaining some of its original form. In solution of red corpuscles by the known proteolytic enzymes the hæmoglobin is attacked and much altered, while it is unaffected in serum hæmolysis. Again, the hæmolysin differs from a ferment, in that definite quantities of complement dissolve definite quantities of corpuscles, and do not have unlimited action as do the ferments; therefore it would seem that the complement enters into combination in the reaction, which ferments do not do.

The origin of the complement is unsettled, although there is much reason to believe that the leucocytes are one source, and perhaps the chief one. The complement content of peritoneal fluid seems to be increased if many leucocytes undergo dissolution in it, and this fact was the basis of the idea of a bactericidal substance, *alexin* (Buchner), that the leucocytes secreted. Ehrlich seems to have demonstrated that this alexin is the same as the immune body and complement, and not a single substance that by itself destroys bacteria. Aseptic inflammatory reactions have been found to increase both the bacteriolytic and hæmolytic complement of the blood, although it cannot be demonstrated that the exuded leucocytes are rich in complement. It has also been found that the complement content of the blood in disease varies often in direct ratio to the amount of leucocytosis. Removal of the spleen does not prevent either the presence of complement or the formation of immune bodies in experimental animals (Levin). Complement is present in the serum of cold-blooded animals.

Undoubtedly there is more than one sort of complement, although at first Ehrlich thought that the complement was one and the same for all cytolytic processes. In some sera saturation of all the complement possible with one variety of amboceptor still leaves the serum

containing complement that can dissolve corpuscles when the proper amboceptors are supplied. Again, serums have been found to possess complements with varying resistance to heat, some being indeed quite thermostable. In one serum, for example, immunized against a mixture of swine, sheep, and ox blood, Wendelstadt found that the complement for swine blood was more resistant to heat than that for ox or sheep blood, while the latter resisted HCl more. Normal horse serum was shown by Ehrlich to contain two complements: one specific for rabbit corpuscles, the other for guinea-pig corpuscles, which could be separated by filtering through a Pukall filter, as the guinea-pig complement alone passed through. This variability in filtration of complement indicates that the size or consistence of the molecules is not dissimilar to that of the enzymes, which are also variously held back by filters. Some complements have been found to diffuse through animal membranes, while others do not. It therefore seems that complement is not, as was at one time believed, a single, non-specific substance, but complements may be as numerous and as various as the intermediary bodies. However, one thing seems proved, namely, that the complement is not developed through the process of immunization, but is a constant constituent of the normal serum, although greatly fluctuating in quantity. In immune serum, as a rule, the amount of complement is inadequate to saturate the immune bodies present. As before mentioned, this deficiency may be met by adding serum from animals not immunized—serum which contains complement. As a rule the normal serum should be from an animal of the same species as the immune animal, but it is a remarkable fact that a proper complement may be obtained for immune serum of one animal from an animal of an entirely different species. For example, serum of a dog immunized against the corpuscles of a guinea-pig, after being rendered inactive by having its complement destroyed by heat, may be again activated by addition of normal guinea-pig serum; that is, the guinea-pig complement will unite with the dog immune body as well as will the complement from the dog.

Another important fact concerning the varieties and nature of complement has been furnished by Kyes, who demonstrated that red corpuscles may contain within themselves intracellular complements, *endocomplement*. Of equal significance is the related observation that *lecithin* will act as a complement for cobra poison. That a definite substance of known chemical composition may act as the complement is an important step, although lecithin must be more allied to thermostable complements than to thermolabile complements, which are the ones seemingly of most importance.

There are two groups in complement: one of which is united to the immune body, therefore a haptophore group, and another that acts upon the cell to which it is anchored, and called the *zymotoxic* group. This latter is analogous to the toxophore group of a toxin. As a matter of fact a complement is a toxin for the cell it may attack. As might be expected, therefore, just as toxoids are formed by degeneration of the toxophore group of the toxin, so also *complementoids* are formed by the degeneration of the zymotoxic group of the complement.

As before mentioned, the affinity between complement and intermediary body is less than between intermediary body and cell receptor, therefore the latter union occurs first. If the amount of intermediary body is largely in excess of the amount of complement the hæmolysis is greatly interfered with, because the excessive intermediary bodies unite with the complement; and as the cell receptors have all been at once occupied by intermediary bodies, the complement cannot become attached to the cell, since intermediary bodies do not unite with each other. This blocking off is referred to as *deviation of the complement*.

Regeneration of complement after it has been exhausted takes place in a short time. In rabbits whose serum was deprived of complement by injecting goat corpuscles until the complement had all been absorbed by them, it was found that complete regeneration may take place in from two to four hours.

Although the complement is the normal, constantly present constituent of the blood that probably protects the body against bacteria and other injurious agents, yet it is also capable of being harmful to the cells of its own creator. Snake venoms, for example, seem to owe their poisonous properties to the presence of large numbers of amboceptors of various sorts, and therefore to produce their violently injurious effects they require the action of complement, which is furnished by the poisoned individual for his own destruction. It is probable that there are other conditions in which the complement is an agent of harm rather than of protection.

The amount of complement in the serum of an individual varies in health, and even more so in disease. In phosphorus poisoning the power of the serum of the rabbit to destroy guinea-pig corpuscles is lost, because the corresponding complement is absent. Longcope claims that complement for typhoid and colon bacilli is decreased in many chronic diseases, which may account for terminal septicæmia. Alcoholism is also said to reduce the complement of the blood of animals. Undoubtedly the fluctuation of complement content of the blood is an important factor in determining susceptibility to infection.

An indication of how purely chemical is the union between the various substances implicated in hæmolysis is the observation by Hektoen that ions of Ca, Sr, Ba, and SO_4 combine in such a way with complement that it is unable to unite with the immune body, and thus they prevent hæmolysis. These inorganic substances seem to saturate the affinity of the haptophore group of the complement in the same way that amboceptors do.

Antihæmolysin.—Just as an antitoxin can be produced by immunizing cells against the toxins that injure them, so by immunizing the blood corpuscles against hæmolytic serum an antihæmolytic serum can be obtained. If heated serum is used an anti-immune body is obtained, that acts by combining with the cytophile group of the intermediary body and thus preventing the intermediary body and the corpuscles from uniting. If there are several intermediary bodies in the injected serum, antibodies may be obtained that are specific for each. These antibodies seem to be the receptors of the red cells that unite with the intermediary body in producing hæmolysis.

By immunizing against normal serum, whether heated or not, *anti-complement* is obtained which also is specific. Ehrlich has shown that this anti-complement acts by combining with the haptophore group, thus preventing the complement from being anchored to the cell by the intermediary body. Such anti-complement does not unite at all with the intermediary body, which remains in a condition capable of taking up fresh complement if it is provided. Again, resembling the production of antitoxin with toxoids, anti-complement can be obtained by immunizing with complementoid.

Not only can *anti-heterolysins* be obtained, but also *anti-isolysins*, if serum hæmolytic for blood of an homologous animal be used in immunizing. Since during normal conditions of life red corpuscles are continually undergoing dissolution, it may be that in everybody there really develop autolysins, which are prevented from causing extensive destruction of the corpuscles by the production of *anti-autolysin*. Besredka seems to have demonstrated the presence of such antibodies in normal serum, and suggests that such self-immunization may be an important process in protection of the body. In this connection it may be mentioned that there seem to be antiferments normally present in the blood that are perhaps of importance in preventing self-digestion of the tissues during life by the ferments of the body itself.

Agglutination in Relation to Hæmolysis.—The well-known agglutinating reactions of bacteria can be duplicated with red corpuscles. As with bacterial agglutinins the agglutinin seems to be, in Ehrlich's terms, a uniceptor; that is, it has but one group with affinity for other substances, as is the case with the toxins. Agglutinins for corpuscles are found to varying extent in normal

serum, as well as in serums specifically immunized against the corpuscles. Heating at 55° C. does not destroy the agglutinin, and in this way the agglutination can be observed independently of the hæmolytic processes. Agglutination also occurs at temperatures approaching freezing, when hæmolysis is inhibited. Agglutinated red corpuscles collect in rouleaux and clumps that unite with considerable tenacity, so that ordinary shaking will not break them up. In hæmolytic immune serum this agglutination precedes the hæmolysis, but the two processes are quite unrelated. Normal serum may contain agglutinins and not be at all hæmolytic, and the converse is also true. The mechanism of agglutination is not understood, but it is suggested that some chemical change in the substance of the corpuscle renders the surface adhesive, or that some physical change in surface tension accounts for the coaptation and adhesion of the corpuscles. As agglutination occurs in corpuscles that have been fixed in formalin or sublimate, it is probably not the proteid of the corpuscle that is affected, but the other ingredients of the stroma, of which lecithins and cholesterin seem to be the chief. Flexner and Noguchi found that if ricin, an agglutinator, was allowed to act for two or more hours it is still possible then to produce hæmolysis by serpent venom, but the stroma remains at the bottom as a white, conglutinated mass. From this it appears that agglutination brings about a kind of coagulation of the stroma.

Agglutination of the corpuscles during life may be of some pathological importance, for such masses of agglutinated corpuscles could readily produce capillary thrombi and emboli, which, if widespread, might create much disturbance. Many bacteria produce substances that are agglutinative for human red corpuscles, among them being typhoid, pyocyaneus, and staphylococcus. Flexner has found in typhoid fever thrombi that seemed to be composed of agglutinated red corpuscles, almost free from fibrin and leucocytes. Probably many of the so-called "hyaline thrombi" found frequently in infectious diseases are really composed of agglutinated, partly hæmolyzed red corpuscles.

Agglutination is also produced by certain vegetable poisons, including ricin, abrin, and crotin, and these have been found to produce thrombi of agglutinated red corpuscles. Of these substances ricin alone, although strongly agglutinative, has no hæmolytic action, showing the independence of the two processes. Snake venom, like most hæmolytic substances, produces marked agglutination, and here also the agglutinin is distinct from the hæmolysin.

(3) Hæmolysis by Bacteria.

Both pathogenic and non-pathogenic bacteria produce hæmolytic substances that are excreted into the fluids in which they grow. During many infectious diseases marked hæmolysis occurs, especially in those with septicæmia. After death the hæmoglobin of the blood goes into solution, and the resulting staining of the walls of the blood-vessels, and later of the tissues everywhere, is generally familiar. In the post-mortem hæmolysis probably the putrefactive organisms are chiefly concerned, although it is marked a very short time after death in many cases of septicæmia, particularly when the infecting organism is the streptococcus, and here probably the pathogenic organism is the chief cause of the hæmolysis. The hæmolytic action of bacteria can be studied both *in vitro* and *in vivo*. Among the best known are *tetanolysin*, *pyocyanolysin*, *typholysin*, *staphylolysin*, and *streptocolysin*, as they have been termed. Of these the case of pyocyanolysin is questionable because it has been described as resisting heat over the boiling point, and Jordan seems to have proved that the hæmolysis is ascribable to the alkalinity that this organism produces in culture media. Other bacterial hæmloysins are, however, destroyed by heat at 70° C. for two hours; that is, they are altogether different from ordinary cellular hæmolysins. G. Ruediger shows the following differences between streptocolysin and the hæmolysins of serum: Streptocolysin is not destroyed at 65° C. for one-half hour, and therefore is different from complement. When destroyed by heating to a higher point it cannot be reactivated by the addition of complement, thus differing from intermediary body. It is also different from intermediary body in that it does not combine with corpuscles at 0° C.; on the other hand it does combine at 6° C., but does not exert any hæmolytic effect until the mixture is raised to a higher temperature. This last observation indicates that the streptocolysin is similar in nature to the toxins, which exhibit the same phenomena. Other observations indicate that its structure is the same as the toxins, namely, a toxophore group and a haptophore group. In other words, streptocolysin is simply a toxin for red cells, which acts like bacterial toxins for other cells by joining directly to the cell receptors without the intervention of any intermediary body. As a similar structure has been shown for staphylolysin and tetanolysin, it is probable that the bacterial hæmolysins are all merely toxins with a particular affinity for red cells.

Secondary anæmia of the infectious diseases is probably to be explained largely by this hæmolytic property of bacterial toxins. Hæmoglobinuria also may be produced in the same way. Intravenous injections of filtrates of the saphrophyte, B. megatherium, will produce hæmoglobinuria in guinea-pigs.

(4) Hæmolysis by Vegetable Poisons.

A number of plant poisons are strongly hæmolytic; among them are phallin and helvillic acids from certain mushrooms; abrin, crotin, agaricin, saponin, solanin, and cyclamin. These hæmolytic poisons are not affected by heating at 100° C., and are therefore quite different from the serum hæmolysins. These substances are at present chiefly of interest from the laboratory standpoint, as being a distinct class of hæmolytic substances. Their mode of action is not clearly understood, but they seem to contain toxophore and haptophore groups like the true toxins.

(5) Hæmolysis by Venoms.

The hæmolytic power of venom derived from different varieties of reptiles has through recent studies been brought into the domain of biologic hæmolysis, and the result has been not only an understanding of the mechanism by which the lethal effect of these poisons is produced, but also perhaps the strongest support of the principles of Ehrlich's theory yet offered from outside sources. At the same time a new, easily controlled medium for research in problems of immunity has been provided. The most fundamentally important fact is the discovery by Flexner and Noguchi that the hæmolytic and other toxic agents of venom are themselves true intermediary bodies. By itself venom is not hæmolytic, but it requires the presence of complement to enable it to produce hæmolysis, and as the venom contains no complement, this necessary part of the poison is furnished by the serum that contains the corpuscles. This is indeed a remarkable fact, that the active part of the serpent's poison is furnished by the victim itself, and particularly so in view of the position that serum complement usually assumes as a protector against bacteria. The existence of a widespread power against various animals implies that these venom intermediary bodies are capable of uniting with the complement of sera of varied animals, are *heterocomplementophilic*, in the language of Ehrlich's theory, and experiment shows this to be true. The probable source of these intermediary bodies is apparently in the serum of the serpents, as if they were secreted directly from the blood into the poison glands, for serum of poisonous snakes is found to possess intermediary bodies almost identical with those of the venom. The only difference is that while venom intermediary body combines with complement of nearly all serums, the serum immune body combines almost only with the complement of the serpent's serum itself (*isocomplementophilic*). Venom from cobra, rattlesnake, moccasin, and

copperhead possesses in each intermediary bodies that seem to be identical in nature, although they may vary in quantity. This explains the rather remarkable fact that serum of animals immunized against cobra poison, generally called *antivenin*, will neutralize the hæmolytic and many of the other properties of the venom of rattlesnake, copperhead, and moccasin. Antivenin acts as an anti-intermediary body, and by occupying one of its haptophore groups prevents it completing the union of complement and cell. In order of decreasing hæmolytic power for mammalian corpuscles come venoms from cobra, water moccasin, copperhead, and rattlesnake. These venoms are also agglutinative for all corpuscles tried, and agglutination will occur at 0° C. Exposure for thirty minutes at 75°–80° C. destroys the agglutinative property. In general, the hæmolytic power of the venoms for different sorts of corpuscles varies in inverse proportion to its agglutinative power. The hæmolytic intermediary bodies are remarkably resistant to heat, suffering but slight loss of power at 100° C. Each venom contains many intermediary bodies, seemingly different for each sort of corpuscle hæmolyzed, at least to a great part; no one sort of corpuscle can so saturate all the intermediary bodies that none is left for other kinds. After the intermediary body is attached to a corpuscle it can unite with many different sorts of complements; but only the one natural to its serum accomplishes complete hæmolysis. Leucocytes also are dissolved, and they seem to have specific intermediary bodies different from those that unite with red corpuscles, but the agglutinin for each seems to be the same. As the venom contains large amounts of intermediary bodies, when an animal is poisoned by a snake the complement is quickly taken up, and this probably explains the deficient bactericidal power of blood serum in this condition that permits the extensive infections so characteristic of snake bites. Antivenin will prevent this interference with normal bacteriolysis by occupying one of the groups of the intermediary bodies of the venom so that it cannot use up the serum complement.

The highly hæmolytic cobra venom can combine with complements contained within the red corpuscles, *endocomplement*, and so produce hæmolysis in the absence of serum complement. Kyes has shown that *lecithin* may be the constituent of the red corpsucles that acts as the complement.

In passing it may be noted that the effects of venom on nerve and endothelial cells, which with the hæmolysis constitute the manifestations of its toxicity, are produced in the same way as the hæmolysis. Amboceptors are present that unite complement to these cells, enabling it to attack them. As certain venoms are richer in one sort of intermediary body than others, so the effects of the bite of one kind of snake differ from those of another kind, *e.g.*, rattlesnake poison is particularly endotheliolytic, and therefore hemorrhages are a prominent sequence of the rattlesnake's bite.

Red corpuscles of the frog are not hæmolyzed by venom, and those of necturus (mud puppy) but slightly, agreeing with the known resistance of cold-blooded animals to snake bites.

Eel serum is remarkably hæmolytic, so much so that a quantity of 0.1 c.c. per kilogram of body weight will kill a rabbit or guinea-pig in three minutes when injected intravenously. Heating at 54° C. for fifteen minutes destroys the hæmolytic action, and, unlike ordinary serum hæmolysins the addition of complement does not restore its activity. Animals can be immunized against this serum. Introduced into the stomach, eel serum is not toxic. It can be dried and redissolved without losing its activity, but acids and alkalies readily destroy it. Mosso, who first discovered the toxicity of eel serum, called the unknown active principle *ichthyotoxin*.

Hæmolysis in Disease.—During health there is always going on a certain amount of destruction of red corpuscles that have outlived their usefulness; so in disease we may have to deal with either an alteration in the normal processes of blood destruction, or the introduction of entirely new processes. Although the place and manner of normal red corpuscle destruction is not completely known, yet it seems probable that there is relatively little hæmolysis within the circulating blood. When a red corpuscle becomes damaged it seems to become more susceptible to phagocytosis, and it is picked out of the blood chiefly by the endothelial cells of the sinuses of the spleen, hæmolymph glands, and bone marrow. Within these cells it apparently undergoes hæmolysis. Eventually the resulting pigment is split up by the liver, the non-ferruginous portion forming the bile pigments, while the iron seems to be mostly withheld to be worked over into new hæmoglobin. Whenever during disease red corpuscles are more rapidly injured than they are under normal conditions, these processes of normal hæmolysis are exaggerated and we not only find the phagocytic cells of the spleen and glands packed with them, but endothelial cells elsewhere and leucocytes also take on the hæmolytic function. At the same time there is an excessive production of bile pigment from the destroyed red corpuscles, which has an undetermined relation to the so-called "hæmato-hepatogenous" jaundice. If hæmolysis is very excessive the blood pigment accumulates in other organs than the liver and spleen. When at one time over one-sixtieth part of the hæmoglobin of the blood is in solution in the plasma, it may escape in the urine, producing hæmoglobinuria.

The hæmolysis of the acute febrile diseases is readily explained by the demonstrable hæmolytic property of the products of the organisms that cause them, such as streptocolysin, staphylolysin, etc. Perhaps at the same time altered metabolic products may also play a part, but it does not seem probable from experimental results that the thermic condition *per se* has much effect. In malaria, although the parasites enter and destroy the corpuscles in which they live, yet this alone does not account for all the blood destruction of the disease, for the amount of anæmia is quite without relation to the number of parasites to be found. There is good reason to believe that the plasmodia produce hæmolytic substances that are discharged into the serum. In the primary anæmias hæmolysis seems to be the essential process, although the agents involved are at present unknown. Absorption of hæmolytic products of intestinal putrefaction or infection has always come in for much suspicion, without ever becoming completely established. Here also the hæmolysis seems to take place in the endothelial cells rather than in the vessels. In such a disease as pernicious anæmia there is much reason to assume that defective or abnormal hæmatogenesis is an important factor. Probably the anæmia of nephritis is the result of hæmolytic action of the retained products of metabolism, in which connection the hæmolytic properties of ammonium compounds may be recalled. In some diseases associated with anæmia it has been found that the blood serum of the patient is distinctly isohæmolytic, although isoagglutination seems to be more frequent. Such sera, however, do not seem to be autohæmolytic, at least in the test tube. The bloody fluids that can be obtained from cancers have been found to be hæmolytic, while antihæmolysin has been found in ascitic and pleural effusions.

In many forms of poisoning hæmolysis is a prominent feature; in some it seems to be the chief effect of the poison, *e.g.*, potassium chlorate and arseniuretted hydrogen. In severe extensive burns there may occur hæmolysis, and hæmoglobinuria may also result. The remarkable "paroxysmal hæmoglobinuria" is at present without satisfactory explanation as to the cause of the hæmolysis. The hæmoglobinæmia of "blackwater fever" has been the cause of much discussion as to whether the malarial parasite or the quinine is the cause, with a divided opinion resulting, although undoubtedly cases do occur in malaria without administration of quinine. After removal of the spleen hæmolysis by the hæmolymph glands exceeds that of the primitive spleen, causing an excessive destruction of red corpuscles (Warthin). This suggests that the spleen may normally dispose of some hæmolytic agent which acts either by stimulating phago-

cytolysis or by so altering the red cells that they are particularly susceptible to phagocytosis.

The lesions produced in the organs of animals injected with hæmolytic agents are usually pronounced and quite characteristic. There is often a subcutaneous œdema, frequently blood-stained, and similar fluid may be present in the serous cavities. The fat is yellowish, and the muscles are darker in color than is normal. The spleen is usually much swollen, soft, friable, and very dark in color. The liver is usually swollen and mottled with red areas in a yellow background. The renal cortex is dark in color, even chocolate-colored, and the pyramids are comparatively light; in the urine is frequently hæmoglobin. In the lungs are often hemorrhages or areas resembling small infarcts. The blood may be thin and even distinctly transparent. Microscopically the red corpuscles are found in all conditions of degeneration, and often fused together. In the liver, besides patches of congestion, fatty changes are present if the animal lives long enough. Large phagocytic cells packed with red corpuscles are abundant in the spleen, as well as diffuse accumulations of blood, often fused, and pigment both free and in the cells. Pigment also accumulates in the renal epithelium, which also often shows much disintegration; congestion is prominent and hemorrhages into both interstitial tissue and glomerules are frequent.

Bacteriolysis.—It is not our purpose in this article to discuss the specific micro-organisms in this relation, but merely to indicate the relations of hæmolysis and bacteriolysis. Whatever has been said in preceding paragraphs about the mechanism of hæmolysis can be transcribed to apply to bacteria and bacteria-immune serum. Pfeiffer's observation of the solution of bacteria by serum of immunized animals was the precursor of the modern studies of hæmolysis and the extension of Ehrlich's theory. Indeed the chief reason for the great interest in hæmolysis lies in the understanding that whatever may be learned about hæmolytic processes can be directly applied to the processes of immunity against bacteria. Therefore we understand that in the serum of an animal immunized against bacteria themselves, and not merely their toxins, there is present an intermediary body that is specific for the injected organism. This intermediary body attaches itself to the bacterium by one haptophore group, and with the other anchors the complement of the serum which then destroys the bacterium. Now as during immunization only intermediary bodies are produced in excess, while the complement is not increased, it often may be that defence may fail because of deficiency in the amount of complement. This possibly explains why it has so far been impossible to secure immune sera that will protect against bacteria as effectively as antitoxin protects against toxin, for with toxin no complement is required. The results of decreased complement content would be an increased susceptibility to infection, and this is seen in snake bites, when the venom uses up the blood complement and the patient often succumbs to bacterial infection after surviving the direct effects of the poison. In chronic diseases Longcope claims that in the later stages the amount of complement is much decreased, probably accounting for the occurrence of terminal septicæmias.

It is probable that hæmolytic complement is quite distinct from that causing bacteriolysis, and that complements for different bacteria can be separated from one another as well as from the agglutinins.

Welch has suggested that possibly the bacteria in their turn may develop antibodies to the tissues and fluids in which they are growing. If so, we have a reasonable explanation of the development of toxic substances with marked action on specific cells of the host, *e.g.*, endotheliolysins, leucolysins, hæmolysins; and also the peculiar manner in which bacteria often attack only certain tissues, *e.g.*, multiple septic arthritis.

Cytolysis.—Red corpuscles being merely a particular sort of body cell it might be expected that lysins for other cells could be obtained in a similar manner, and such is the case. Such lysins are called by the generic term *cytolysins*, or *cytotoxins*, and are specifically indicated by the name of the cell concerned, as endotheliotoxins or endotheliolysins, hepatotoxins, nephrotoxins, etc. The lysins or toxins in this case are similar in composition to the hæmolysins, that is, an amboceptor and a complement group, and these groups are in all respects similar to the components of the hæmolysins except that the cytophile group of the amboceptor is specific for certain tissue cells rather than for red corpuscles. Such specific cellular toxins may be obtained by immunizing the animals against the tissue which is injected emulsionized into its peritoneal cavity; but, as with the hæmolysins, they may occasionally appear in normal serums of various sorts of animals. It is by no means as easy to determine the results with tissue cells as with red corpuscles, where the liberation of the highly colored hæmoglobin is easily detected. To some degree lytic changes can be observed in tissue cells under the microscope, but this is not usually very satisfactory. Another method of observation consists in injecting the immune serum into the body of an animal, and studying both the symptoms and the anatomic changes brought about in this way. The latter method has found the most general application. A disturbing element in all such experiments lies in the difficulty of securing tissue cells of one kind alone for injecting. For example, when hepatic-tissue suspensions are injected there are introduced at the same time endothelial cells, connective-tissue cells, and usually red corpuscles and leucocytes. Therefore an immune serum obtained in this way would contain immune bodies for all these cells, and it becomes impossible to ascribe any changes that follow its injection into an animal solely to effects of the hepatotoxins. While there are possible ways of avoiding many of these difficulties they have not been generally applied, and much of the earlier work is very questionable on this account. At the same time that cytolysins are formed agglutinins also appear, and agglutination of specific cells occurs as it does with bacteria and corpuscles. One of the earliest pieces of work in this direction was with sperm agglutinins, obtained by immunizing with sperm. Such serum, however, was not spermolytic. In view of the elementary condition of cytolytic investigations, and the afore-mentioned sources of error in much of the work that has already been reported, I do not feel justified in this article in more than briefly discussing the specific results so far obtained. It should also be mentioned that recently some investigators who have used care in avoiding hæmolysins, etc., in preparing specific sera have not been able to obtain as marked results as had been earlier reported.

Leucocytolytic Serum.—This may be obtained either by immunizing with leucocytes obtained from exudates or from the blood, or by using emulsions of lymph glands. The latter method introduces so many cells besides the lymphocytes that it is not desirable. Specific leucocytolytic sera agglutinate leucocytes and produce observable morphologic changes, in the way of solution of the cytoplasm and cessation of amœboid movements. Of the leucocytes the large granular cells seem most affected and the lymphocytes least. When injected into the peritoneal cavity such serum causes an apparent initial leucopenia, and later a decided leucocytosis in the peritoneal fluid. Corresponding with this, if bacteria are injected at the same time as the serum, resistance is found decreased, but later it is much increased. Such serum also contains anticomplement, according to Wassermann, indicating that the injected leucocytes contain complement. Leucotoxin obtained by immunizing against lymphatic tissue is very thermolabile, being destroyed by 55° C. for thirty minutes, and the serum can be only partially reactivated by the use of fresh serum. Undoubtedly leucotoxic amboceptors are present in many normal sera, and their presence in the serum of certain cold-blooded animals and in venom has already been shown.

Endotheliolytic Serum.—Every attempt at immunizing an animal with any sort of fixed tissue must of necessity

involve the injection of endothelial cells as well as those specific to the tissue studied. Therefore it is possible that cytotoxic serum so obtained will contain endothelial toxins and so complicate any results of *intra vitam* experiments. There is every reason to believe that endotheliolytic substances are produced in this way. Ricketts found that serum of animals immunized against lymph glands was toxic to endothelial cells, which was indicated by hemorrhages at the point of injection, and marked desquamation of endothelium when the injection was made into a serous cavity. In snake poisoning the extensive hemorrhages are also due to an endotheliolytic principle, called by Flexner *hæmorrhagin*. This is destroyed by heating at 75° C., and is particularly abundant; in fact, the chief toxic agent in rattlesnake venom.

Lymphatolytic Serum.—This serum has been studied recently by Ricketts and by Flexner, immunizing animals with lymph glands. As might be expected from the nature of the injected glands the resulting serum contained endotheliotoxin, leucotoxin, hæmolysin, hæmaglutinin, leuco-agglutinin, and precipitins. When injected into animals this serum had a marked effect upon the spleen and lymph glands, producing great enlargement of these structures, which were also congested. The bone marrow was also somewhat affected, and when marrow was used in immunizing, the *myelotoxic* serum produced marked proliferative changes in the lymph glands as well as in the marrow. The changes produced in the leucocytes were the same as those described for leucotoxic serum, indicating that the different forms of leucocytes can combine with immune bodies produced against lymphocytes.

Nephrolytic Serum.—It has been claimed that if a kidney is destroyed by ligating its vessels or ureter the remaining kidney develops serious degenerative changes, which are not present if one kidney is entirely removed. This has been attributed to the development of nephrotoxic substances produced in reaction to the absorption of the injured renal tissue that has been left in the body. Other methods of renal injury have been thought to produce similar effects, and serum of animals with kidney disease was said to injure the kidneys of normal animals. From this basis it has been thought to explain the progressive nature of the chronic nephritides as the result of nephrotoxins produced through the absorption of the injured cells, and which nephrotoxins injure still other cells. Such a process, however, involves the production of cell toxins in an animal toxic for its own cells, that is *autocytotoxins;* and as it has so far been practically impossible to produce autolysins of other sorts, it is not altogether probable that the kidney is an exception. Furthermore, the latest writer, Pearce, was unable to produce *isonephrotoxins*, and could not corroborate the results said to have been found in the remaining kidney after ligating the vessels of the other. He did obtain an active *heteronephrolysin*, but also found that immunization with liver produced just as actively nephrolytic serum as immunization with kidney.

Neurolytic Serum.—Even so highly specialized cells as those of the nervous tissue seem to produce a reaction with the formation of immune bodies. Perhaps because any symptoms produced by action on the nervous system are so readily detected, and because of the advanced condition of our knowledge concerning the minute structure of ganglion cells, the results obtained with neurolytic serum have been particularly striking. Perhaps the most positive results are those of Ricketts and Rothstein, who found that serum of rabbits immunized against the brains or cords of guinea-pigs, when injected into the vessels of guinea-pigs was highly toxic, causing death with various symptoms only explainable on the assumption of nervous lesions. Microscopically the ganglion cells showed marked changes in those animals that survived the injection long enough. All the results so far obtained have been with heterogeneous serum. Venoms, particularly that of cobra, possess strong neurolytic substances, that are the chief toxic agents in most of the venoms (the rattlesnake excepted). This neurolysin can be removed by saturation with nervous tissue from the hæmolysin, and conversely the hæmolysin can be removed by saturating with red corpuscles, thus corroborating Wassermann's experiments with tetanus toxin and supporting Ehrlich's theory.

Thyrolytic Serum.—There are but few reports on this serum, but of these the latest, that of Portis, indicates that after removal of all hæmolysis as a factor there do occur changes in the nature of excessive absorption of colloid, and proliferation after the order of that seen in regeneration. However, the clinical picture of thyroidectomy was not produced in any case, and the anatomic changes were not great.

Numerous reports may be found indicating attempts with varying success to obtain sera toxic for other tissues. Among them may be mentioned *epitheliolysin* (for ciliated epithelium), *spermatotoxin*, *hepatolysin*, *cardiolysin*, *splenolysin*, and *syncytiolysin*. Attempts at the production of immune serum with adrenal by Abbott resulted only in a serum with great hæmolytic power, but with no particular effect on the adrenal. The principle in all is the same, but the results as a whole are not now in a state to warrant extensive consideration. In general, it can be said that it has not been found possible in this way to throw out of function one particular organ, with or without involvement of other structures. It must be borne in mind that we can have grave functional disturbances without corresponding anatomic alterations. There is no reason known why a group of receptors of essential importance to the functional manifestations of the cell may not be quite independent of vegetative functions; and with impairment of these alone there need be no visible cell changes. *H. Gideon Wells.*

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References to all the later literature of importance will be found in the reviews of pathologic literature by Hektoen, in Progressive Medicine, each year since 1900.

HEMLOCK, POISONING BY.—The water hemlock (*Conium maculatum*) is a small herb, belonging to the natural order *Umbelliferæ*. It must not be confounded with the hemlock tree (hemlock spruce), a well-known product of the forest regions of the United States. Conium maculatum is indigenous in Europe, but has established itself to a limited extent in other countries. It is regarded as the poison which was used by the ancient Athenians in putting to death certain criminals, and has become famous in consequence of its use in the case of Socrates.

The poisonous properties exhibited by several parts of the plant, especially the fruit, are due to several alkaloids, of which coniine (sometimes called coniin) is the most important. This is a distinct alkaloid, forming a series of salts, and is one of the few of its class that are liquid at common temperature and do not contain oxygen. Its formula is $C_8H_{17}N$. It is a colorless liquid, specific gravity about 0.880, not very soluble in water. It boils at a temperature considerably above that of water, and has a distinct rotatory action on polarized light. Its odor is usually said to be mouse-like, a rather vague description, but it cannot be more directly described, except to say that it is strong and disagreeable.

Cases of hemlock poisoning have been mostly accidental, parts of the plant having been mistaken for edible herbs, such as parsley. The recorded cases give diverse symptoms, and it is highly probable that mistakes have been made as to the identity of the plants in several instances. The following summary represents the marked features: Headache, vertigo, dilated pupils, a prickling sensation in the extremities, with gradually developing paralysis. This latter usually begins in the legs. The paralytic condition extends to the muscles of the trunk and neck, speech and deglutition become im-

perfect, and finally asphyxiation may occur by failure of the respiratory muscles. The mind is not much impaired until the latest stages of the case. Convulsions may occur at an advanced stage. A case may last several hours, but is likely to be much more rapid in its progress, death sometimes occurring in a few minutes. The poisonous dose is small, but cannot be accurately fixed from the data at hand. Probably one drop of coniïne would be fatal to an adult in most instances if treatment was not promptly instituted.

Treatment must be of the type used for the alkaloids in general. Tannin and animal charcoal have some antidotal value, but the thorough washing out of the stomach will be found to be of most advantage and should be instituted as soon as possible. Artificial respiration may be required in the advanced stages of the case. The marked paralytic condition suggests the use of strychnine in very small doses hypodermically, but such treatment must be used with caution.

The detection of the characteristic alkaloid is a difficult matter, but its peculiar odor will be of value. More important, from a practical medical point of view, is the recognition of parts of the plant. These should be carefully examined, and compared with authentic specimens, or mistakes will be made, for species of Umbelliferæ are often difficult to differentiate. The post-mortem appearances are not characteristic. *Henry Leffmann.*

HUNYADI JANOS SPRING, AUSTRIA.—A mineral spring at Ofen, Hungary, a part of Budapest. The water bearing this name, so universally used, especially in this country, is one of the "Hungarian bitter waters"; others, almost as well known and obtained from the same locality, are the Franz-Josef and the Apenta. These three are the strongest of the bitter mineral waters, and are used either as a laxative or as a cathartic, the effects depending upon the quantity of the water taken. The active ingredients are the sulphates of sodium and magnesium. The following table shows the proportions in which they occur in the various Hungarian waters; and, for purposes of comparison, several other waters of like constituency are included.

ONE LITER OF WATER CONTAINS:

	Sodium sulphate. Grams.	Magnesium sulphate. Grams.
Hunyadi Janos	22.55	22.35
Franz-Josef	23.18	24.78
Apenta	15.40	24.40
Pullna	9.59	10.85
Friedrichshall	6.05	5.15
Kissingen Bitterquelle	5.80	5.00

The following is an analysis of the Hunyadi Janos water by Professor Bunsen. One pint contains: Sodium carbonate, gr. 13.20; ferrous (oxide) carbonate, gr. 0.08; calcium carbonate, gr. 6.04; strontium carbonate, gr. 0.19; sodium chloride, gr. 11.54; potassium sulphate, gr. 1.67; sodium sulphate, gr. 128.97; magnesium sulphate, gr. 137.98; silicious earth, gr. 0.09. Total, 299.76 grains. Free and partly combined carbonic acid, 8.06 cubic inches.

Other well-known waters of like character are those of the Rubinat Condal, Rubinat Serre, and Rubinat Llorach Springs in Spain.

The taste of these waters is disagreeably bitter, much like a solution of "Epsom salts," although it is said to be somewhat modified by the presence of free carbonic acid and the other salts; at best, however, they are not a pleasant drink.

These sulphated bitter waters are much employed either as an occasional aperient, or in habitual constipation and in dyspepsia accompanied by constipation. They are also a serviceable laxative in small doses in pregnancy, arteriosclerosis, cardiac disease, and other morbid conditions in which an unstimulating laxative is desired. In large doses they are indicated where a rapid, full evacuation of the bowels is the end in view. In brief, in all the innumerable conditions in which a "dose of salts" is indicated, these bitter waters, which are practically a solution of salts, can be used. The usual dose of the strong bitter waters is from a half to one wineglassful taken on an empty stomach. In emergency cases a larger dose can be taken—from three-quarters to one tumberful.

Edward O. Otis.

IRON, POISONING BY.—Metallic iron and those compounds of iron which are insoluble in water are not poisons. The soluble salts, however, though not active poisons, have an irritant action, and are capable of destroying life when taken in large doses and in a concentrated state. The continued administration of medicinal doses even produces, after a time, decided gastric disturbance. It is probable that all the soluble preparations may act as irritant poisons when administered in large doses. The most important, however, from a medico-legal point of view, are ferrous sulphate (copperas, green vitriol), ferric chloride (perchloride), which is used medicinally in the form of tincture, and the tannate in the form of ink.

The salts of iron are rarely administered for criminal purposes. Most of the reported cases of poisoning have been the result of accident, or of the use of the sulphate or the tincture of the chloride of iron in attempts at abortion. The symptoms which follow the administration of large doses of the preparations named are essentially similar to those produced by the irritants in general. There are a styptic taste in the mouth, nausea, vomiting, pain in the stomach and intestines, and purging. The evacuations are black, owing to the conversion of the iron salt into a tannate by the tannic acid of the food, or into a sulphide by the sulphureted hydrogen resulting from decomposition in the intestines. Irritation of the genito-urinary passages is sometimes observed. The tincture of the chloride of iron is more corrosive in its action than the sulphate, by reason, apparently, of the free hydrochloric acid which it frequently contains. Its injection into the cavities of the body, for the purpose of arresting hemorrhage, has proved fatal.

The amount of any of the preparations of iron required to endanger life is not accurately known, but appears to be quite large. In most of the cases in which the sulphate has been taken, the amount was unknown. Recovery has taken place after a dose of 31 gm. (℥ i.) of the sulphate (Christison). A case is reported in which 48 gm. (fl ℥ iss.) of the tincture of the chloride of iron proved fatal in about five weeks (Christison). Recovery has taken place after doses of 32–96 gm. of this preparation. The favorable issue is probably due, in many cases, to the early occurrence of vomiting.

The results of experiments on animals are not uniform. Gmelin states that 7.7 gm. (℥ ij.) of the sulphate of iron administered to dogs by the mouth caused vomiting only; that 2.6 gm. (gr. xl.) administered to rabbits produced no injury; and that 1.3 gm. (gr. xx.) injected into the veins of a dog produced no symptom whatever. Dr. Smith, however, states that 7.7 gm. will prove fatal to dogs when administered by the mouth or applied to a wound.

The post-mortem appearances are those of a simple irritant, and are confined, so far as has been observed, to the stomach and upper part of the intestines. In acute cases the contents of the intestines will probably present a black appearance, owing to the presence of the tannate or the sulphide of iron.

Iron is eliminated to some extent in the urine. A small amount only is absorbed in any event, the greater part escaping in an insoluble form with the fæces.

Treatment consists in the use of the stomach-pump, or of emetics if necessary. Magnesia or dilute solutions of alkaline carbonates should be administered as antidotes, and these should be followed by demulcents.

William B. Hills.

LIPOMA (Adipoma, Steatoma) is a tumor consisting essentially of adipose tissue. Such growths belong to the mature connective-tissue tumors, and have for their

physiological prototype the adipose tissue found beneath the skin and serous membranes. Between normal adipose tissue and the fat tissue of lipomata there are no essential differences of structure. In the majority of lipomata the fat cells as well as the fat lobules are usually larger than those of normal adipose tissue (the former three to four times as large); but this difference does not hold good to such an extent that it can be used as a point in differential diagnosis. In general, a lipoma presents the structural characteristics of a localized mass of fat differing in no respect from normal subcutaneous fat. The chemical reactions of the fat contained in lipomata likewise correspond to those of normal fat.

Since the resemblance in structure to normal adipose tissue is so very close, it may sometimes be difficult to draw a line between a simple hypertrophy of adipose tissue and a lipoma. Both general and local hyperplasias of adipose tissue occur which are not classed with lipomata (general lipomatosis, lipomatous elephantiasis, the deposit of fat about an atrophic kidney or between the bundles of atrophic muscles); but other local hyperplasias of a similar nature have by various authors been styled lipomata. Thus the hyperplasia of the fatty capsule of the mammary gland which occurs sometimes in scirrhous carcinoma of this organ or in chronic interstitial mastitis has been called *lipoma capsulare*, an excessive deposit of fat beneath the epicardium has been styled *lipoma cordis capsulare*, and the deposit of fat in the villous fringes of the joints is known as *lipoma arborescens*, although analogous to the fatty hyperplasia so frequently seen in the epiploic appendages of the large intestine. Such local fatty hyperplasias may be styled *pseudolipomata*. An exact use of the term lipoma would limit its application to those formations of adipose tissue alone in which an actual new formation of fat tissue occurs. Such a criterion has, however, but little practical value, since in the fully developed growth of fat tissue it may be impossible to say whether the latter has arisen from a circumscribed hyperplasia or represents a true neoplasia. This difficulty is increased by the fact that lipomata are usually found in those parts of the body in which there is normally more or less fat tissue. A more practical guide will therefore be found in the principle that the term lipoma should be applied to *circumscribed proliferations of adipose tissue which show a certain anatomical and physiological independence of the neighboring tissue, even when the latter is fat tissue*.

The application of the term lipoma made by some writers to tumors other than connective tissue, the cells of which have undergone fatty degeneration or contain an abundance of fat, is wholly incorrect. The true lipomata belong to the mature connective-tissue tumors —that is, the tissue of which they are composed is of the type of adipose tissue.

Histogenesis.—The histogenesis of lipomata is not yet definitely known. Their very frequent development in regions where fat tissue is normally found has led to the belief that the majority arise from a hyperplastic proliferation of adipose tissue with new formation of fat cells and fat lobules. Such an explanation would hold good even for the lipomata which are sometimes found in the submucosa of the gastro-intestinal tract, since in well-nourished individuals fat cells are usually present in small numbers in this region, and from these a lipoma could take its origin. Another view is that lipomata arise from undifferentiated embryonal cells which have persisted from fœtal life, or are formed by the proliferation of connective-tissue cells. The development of fat tissue from these follows the same course as that of the normal development of fat cells from fœtal myxomatous tissue. It is not improbable that undifferentiated "primitive fat organs" (developing fat lobules in the fœtal mesenchyma) may persist quiescent until adult life and later resume active proliferation, giving rise to localized growths of fat tissue which in their development would be more or less independent of the normal laws of nutrition and cell growth. Support is given to this theory by the fact that some lipomata in their growth appear to be entirely independent of the laws governing the general nutrition of the body, since they continue to increase in size or at least do not become smaller under conditions of cachexia, etc., when the normal fat tissue is being reduced in amount. The fact that a combination of myxomatous tissue and adipose tissue is frequently found under pathological conditions may also be taken as an indication of the close histogenetic relations of these tissues. In many lipomata areas of myxomatous tissue occur, and occasionally the appearances presented suggest the development of the fat tissue out of the myxomatous. Moreover, there are rare forms of lipomata in which the fat cells resemble those of embryonic adipose tissue, in that the fat droplets are of small size and do not coalesce into larger drops filling the entire cell.

A further origin for lipomata may be found in atrophic lymphadenoid tissue, a physiological paradigm being found in the development of fatty marrow from the lymphoid marrow, and the fatty transformation of the thymus, and later in old age that of the lymphatic glands. The relationship between lymphoid tissue and adipose tissue is very close. In the fœtus the development of the lymph glands is either coincident with that of the primitive fat organs or follows it; in the latter case the lymphadenoid structures (both ordinary lymphatic and hæmolymph nodes) developing out of the fat organs. In adult life under certain conditions a new formation of lymph glands takes place from adipose tissue, and in old age the lymph glands become to a large extent replaced by fat tissue. Throughout life it is very probable that there is a constant cycle of alternation between lymphoid tissue and adipose tissue. As the result of some disturbance of these processes it is possible that lipomata may arise, either from atrophic lymph glands or from anlage of undifferentiated cells. Askanazy traces the origin of multiple lipomata in particular to a replacement of lymph glands by fatty tissue.

The lipomata of the uterus, kidney-cortex, brain, spinal cord, etc., are to be referred to misplacements of anlage of fat tissue or of fibrous connective tissue which later undergoes a fatty metaplasia. Such lipomata are to be classed with the heterotopous teratomata. It should be borne in mind also that lipomatous masses not infrequently form the bulk of teratomata found in other regions as well.

Etiology.—As in the case of the other true neoplasms but little is known of the etiology of lipomata. Some of them may arise as the results of trauma or chronic inflammation. Such an origin has been ascribed to the fatty tumors sometimes found in the hands of working people in the parts most exposed to injury. In other cases fatty tumors have been found developing from scars. The fatty growths in the villi of the joints are usually associated with a chronic arthritis. There also seems to be some association between multiple lipomata and rheumatoid affections. In the case of the multiple and symmetrical lipomata a nervous or trophic origin is assumed by many writers. In such cases other symptoms suggesting a neuropathic origin are not infrequently present. According to Grosch, multiple lipomata of the skin arise from a disturbance of fat secretion by the skin glands due to a trophoneurosis. A connection between lipomata and disease of the thyroid and hypophysis has also been assumed by some authors. In the majority of cases it is very probable that lipomata are to be regarded as congenital, that is, they arise from misplaced anlage. A tendency to the development of lipomata appears also to be inherited in some families.

Gross Appearances.—All lipomata possess a more or less definite capsule. In the sharply circumscribed forms the capsule may be well defined, of varying thickness; in the diffuse forms the capsule is not perfect and often sends prolongations of connective tissue into the surrounding tissues, which if not removed may lead to a recurrence of the growth. The size of lipomata varies greatly; in the kidney, submucosa of the intestinal tract, etc., they may be very small, while in the subcutaneous tissues of the shoulder and back and in the retroperito-

neal tissues they may give rise to tumors weighing fifty pounds or more. As a rule, they do not exceed ten pounds in weight. They usually form lobulated growths of more or less regular contour. A subdivision of the larger lobules into smaller ones gives the growth a tuberous appearance. Lipomata are not infrequently pedunculated, particularly those found in the submucosa of the alimentary tract, though even in the skin the tumor may occasionally possess a relatively long and narrow pedicle (*lipoma pendulum*). Accessory nodules are rarely seen about the main growth. In the majority of cases lipomata are solitary. Occasionally they are multiple, and in such cases the tumors may be symmetrically distributed over the body. As a rule, lipomata are soft, elastic, and may give a sensation of fluctuation. Puncture with a trocar yields no fluid except in those cases in which extensive retrograde changes have taken place. The absence of fluid on aspiration may therefore have a certain diagnostic value. The occurrence of retrograde changes may render the growth either harder or softer. As a rule, the cut section of a lipoma presents a yellowish or whitish, glistening, lobulated surface, having the characteristic appearances of adipose tissue. In the majority of cases the microscopical examination is hardly necessary for the diagnosis.

Microscopical Appearances.—As stated above, the minute structure of lipomata corresponds in general with that of normal subcutaneous fat. Other varieties of tissue may take part in the make-up of the growth. If the fibrous trabeculæ are developed to such an extent that they form a prominent feature of the tumor the latter may be styled a *fibrolipoma*. As the result of the increased consistence of such tumors they are also called *lipoma durum* or *steatoma*. A combination of myxomatous tissue with fatty tissue gives rise to a *myxolipoma*. *Osteolipomata, chondrolipomata,* and *myolipomata* have also been described. An abundant blood supply with overdevelopment and dilatation of the blood-vessels gives rise to the form known as *teleangiectatic lipoma;* the formation of blood spaces resembling those of erectile tissue to the variety known as *lipoma cavernosum*. The soft form of fibroma may also be combined with a lipoma. To very cellular varieties of a sarcomatous nature the term *liposarcoma* may be applied. Such forms are rare, sarcoma developing less frequently in lipoma than in any other benign connective-tissue tumor. In rare cases an excessive formation of fat of lipomatous nature may be combined with sarcoma or carcinoma. Lipomatous formations are not uncommon in teratomata, and may form the bulk of the tumor. The presence of other histological elements such as epithelial and nervous tissues gives a basis for differential diagnosis. Varieties of lipomata have also been described in which the fat tissue presented the appearances of embryonic adipose tissue.

Evidences of the growth of the lipoma may be found either in the capsule or in centres of growth which are scattered throughout the tumor. The new formation of adipose tissue may therefore take place peripherally or at different places in the tumor. A fibrous connective tissue is usually first formed, and this later undergoes metaplasia into fat tissue.

Manner of Growth.—According to their manner of development lipomata may be classed as *solitary, multiple, circumscribed, diffuse, symmetrical,* etc. The diffuse and multiple forms are closely related on the one hand to the simple hyperplasias of fatty tissue resulting from anomalies of metabolism, overeating, etc.; and, upon the other hand, to the multiple fibromata, chondromata, osteomata, etc., which are congenital or develop from misplaced anlage.

The *diffuse* and *multiple* lipomata, particularly the *symmetrical* forms, have in recent years attracted much attention, and various hypotheses have been advanced in explanation of their origin. In certain cases there appears to be some definite connection between disturbances of the nervous system and the development of multiple lipomata. Numerous clinical observations show the coincidence of occurrence of multiple lipomata and nervous conditions. The development of symmetrical lipomata in association with disturbances of sensation and motion has been seen in the lower extremities after injury to the spinal column. Neuralgias, trophic disturbances of the skin, etc., have been observed in connection with multiple and symmetrical lipomata. It is probable of course that in some of these cases the nervous disturbances may be the result of pressure by the tumor. Lipomata which are themselves painful are also seen. In such tumors there may be a new formation of nerve fibres, or the tumor may spring from the connective-tissue sheaths of the nerve trunks or the symptoms may be the result of pressure. An exact anatomical distribution of the tumors to accord with the peripheral nerves cannot always be made out. Multiple lipomata may also be inherited. Blaschko reports the case of a family in which the male members developed multiple lipomata at the age of puberty, while the females were not affected. The coincidence of multiple lipomata with rheumatoid affections has already been mentioned.

Broca has reported an extraordinary case of multiple lipomata. In a man of the age of twenty-five years there appeared on the right thigh a small fatty tumor which in six years attained a large size. It was excised, found to weigh five pounds, and to consist of ordinary adipose tissue. The patient remained well for five months when there occurred an eruption of hundreds of small fatty tumors all over the body, fresh ones developing from time to time during a period of forty years. At the age of seventy the man came under Broca's care for treatment for dysphagia. Two thousand and eighty tumors in size from that of a pea to that of a walnut were counted over the body, more minute ones not being included. The original scar showed no signs of disease. The microscopical examination of portions of the growths removed during life gave the appearance of lipofibroma. Increase of dysphagia caused emaciation to set in. This at first did not affect the tumors, but after several weeks the emaciation became extreme and the tumors diminished. The patient finally died of starvation. At autopsy no trace of fat was found in the normal fat depots. A large fatty tumor surrounded the œsophagus for the greater part of its extent, occluding the lumen; the pylorus was surrounded by a similar growth. Fatty growths were found in the valves of the heart, in the deep tissues of the neck, in the sheath of the carotid vessels, and in the sheaths of the muscles, as well as in the normal fat regions. Many of the tumors had lost their fat, they consisted of fibrous tissue; the others presented the appearances of fibrolipomata. It is difficult to explain such a case as this except on the ground of a congenital anomaly.

Site.—Lipomata are found most frequently in those parts of the body where fat tissue is most abundant normally: in the subcutaneous, subserous, and submucous fat, and the intermuscular connective tissue, and less frequently in the kidney, periosteum, joints, tendon sheaths, meninges, etc.

Subcutaneous.—Circumscribed lipomata are found more frequently in the subcutaneous tissues than elsewhere, appearing as movable, lobulated, elastic tumors. The neck, back, gluteal region, thighs, axillæ, anterior abdominal wall, arms, hands, and feet are mentioned in the order of frequency of involvement. Lipomata of the scalp and face are rare. The palms of the hands are more often the seat of fatty tumors than the soles of the feet. In the hands lobules of fat may extend from the main mass of the tumor underneath the palmar fascia. Small lipomata may be found occasionally on the fingers. In regions where the skin is loose the lipoma may become pedunculated. Subcutaneous fatty tumors may reach a very large size. They are sometimes painful and may be associated with nervous symptoms. Ordinarily they are painless. Over the large ones the skin may be stretched to such an extent that it may become very atrophic or may undergo ulceration. In this way the tumor itself may become infected. The loose nature of the fatty tissue and the low resistance of the surrounding

tissue make such an infection dangerous, as it is very likely to become phlegmonous.

The diffuse pseudolipoma of the subcutaneous tissue of the neck may be mentioned here. It is in reality a diffuse fatty hyperplasia and gives rise to the condition known as "fatty collar." The deeper fascia may also be involved, and the lipomatosis may spread over the back, shoulder, and trunk. Similar fatty hyperplasias may occur in the subcutaneous tissue in other parts of the body. In some cases they are symmetrically arranged. In the majority of these cases there seems to be a definite connection between the condition and chronic alcoholism. Under changed conditions the fatty deposits become smaller. The diffuse, multiple, and symmetrical fatty deposits are therefore better classed as pseudolipomata.

Subserous.—Small lipomata are not rare in the subserous tissues. Polypoid fatty growths are occasionally seen in the peritoneum, pericardium, pleura, and the synovial membranes. When possessing a definite pedicle the latter may become twisted and atrophy, or may tear, setting the tumor free into the serous cavity where it appears as a free mass of fat showing more or less calcification. The subserous lipomata may reach a large size, particularly in the retroperitoneal region, and may become dangerous through the pressure exerted upon important organs. Adami has discussed at length the subject of retroperitoneal lipoma, collecting forty cases from the literature and reporting several of his own. As a rule, the fatty tumors of this region are slowly growing, but may attain a very large size. They are usually situated more to one side than to the other, and are usually crossed by some portion of the large intestine. Since they give fluctuation they are generally at first mistaken for cystic tumors, but puncture with the trocar yields no fluid. This fact is the most important point in the differential diagnosis. Small fatty tumors are sometimes seen in connection with femoral and inguinal hernias, but these are more of the nature of local hyperplasias of fat tissue than of true neoplasms. Such hyperplasias may in themselves constitute the hernia, and may drag the intestine down into the sac (hernial lipomata). Similar hyperplasias of the epiploic appendages may present the appearance of pedicled lipomata. Subserous lipomata of the anterior abdominal wall may sometimes appear as subcutaneous tumors as the result of the atrophy or displacement of the abdominal muscles. Large fatty tumors of the omentum have also been reported; in several instances the growth presented the character of a myxolipoma.

Submucous.—Small pedicled lipomata of the gastrointestinal submucosa are occasionally found. They are usually of small size, and rarely give rise to symptoms. In a few cases they have been of the size of a man's fist, and when situated at the pylorus or ileocæcal valve, caused obstruction. In other cases they have led to intussusception. In the submucosa of the respiratory tract fatty tumors are more rare. Fatty polypi are sometimes seen in the laryngeal and nasal mucosa.

Intermuscular.—Fatty tumors are occasionally found between the muscles, arising in the intermuscular connective tissue. They may reach a very large size. The myxolipoma is the most common form, and is characterized by a tendency to become sarcomatous. They are found most frequently in the gluteal folds, thigh muscles, and muscles of the neck. Congenital lipomata have been found in the muscles of the anterior abdominal wall. Enlargement of the sucking disc may give rise to a lipomatous tumor.

Periosteum.—Lipomata of the periosteum are rather rare. As a rule, they also contain striped muscle fibres, and are therefore to be regarded as heterotopous teratomata. In some cases parosteal lipomata have been observed at birth.

Joints.—A diffuse subserous hyperplasia of fatty tissue is not uncommon in the synovial membranes of the joints, the knee- and shoulder-joints being most frequently affected. The hyperplasia of the villous fringes gives rise to an arborescent appearance (*lipoma arborescens*). The movements of the joints may be affected. These conditions are not to be classed with the true lipomata.

Internal Organs.—Lipomata are found most frequently in the kidneys than in any other of the internal organs. The tumors may arise either from the fatty or fibrous capsule, or from the interstitial connective tissue of the

Fig. 5158. Fibrolipoma of the Kidney. (Nauhan.)

cortex and medullary pyramids. They are usually of small size, but occasionally become so large as to be of clinical importance. In the capsule the tumors may represent local fatty hyperplasias or metaplasias; in the kidney cortex they are probably heterotopous teratomata, though it is possible that they arise in some cases directly from the interstitial connective tissue of the organ or represent a metaplasia of a fibroma or of a mass of scar tissue. Many growths described as kidney lipomata were in reality "adrenal rests." The writer has reported a unique case of fibrolipoma of this organ which was so large as to cause serious clinical symptoms and to require operative interference. The growth, of which an illustration is here given (Fig. 5158), was a lobulated mass fourteen inches long, eight inches wide, and six inches in thickness, weighing two pounds. It completely filled the enormously dilated pelvis of the left kidney, and sent a round cord-like prolongation down into the dilated ureter. The only remains of kidney tissue were found microscopically in the cyst wall enclosing the tumor, which was entirely free except for a pedicled attachment posteriorly. At this point the tissues of the tumor passed into those of the cyst wall. Microscopically the tumor presented the structure of an œdematous fibrolipoma, its surface being covered with a layer of atrophic transitional epithelium derived from the kidney pelvis.

Lipomata of the *heart* are very rare. The majority of cases reported as such were most probably conditions of excessive fatty infiltration. According to Orth, small lipomata are sometimes found under the epicardium near the apex. Albers, Banti, Handford, Pasini, and others have reported the occurrence of lipomata arising in the intermuscular connective tissue. The cases described as lipomata of the *liver* and *spleen* are very doubtful. Those found upon the capsule of these organs probably represent portions of omentum or epiploic appendages that have become loosened. A formation of adipose tissue may occur also in old adhesions. Lipomata of the *ovary* have apparently not yet been observed. In the *uterus* tumors of the nature of lipomyoma or fibrolipoma have been seen in a few cases. Fatty tumors of the *broad ligament* are very rare. Very large lipomata are occasionally seen in the *vulva*. They may increase in size during pregnancy. Small ones are found rarely beneath the skin of the *scrotum*. Connected with the *spermatic cord* there are found sometimes lipomata of considerable size. Some of the smaller tumors of the cord described as lipomata may have been adrenal tissue (adrenals of Marchand). In the *central nervous system* lipomata are found rarely. They arise usually from the meninges, but fatty tumors have been found in the substance of both brain and cord. In the case of the brain, they appear to be found most commonly in connection with the corpus callosum. They are probably of the nature of heterotopous teratomata. In the complex teratomata of the nervous system a large part of the tumor mass may be made up of fat tissue. Fatty tumors are also not infrequently found in the sacral and lumbar regions in connection with spina bifida occulta.

Retrograde Changes.—According to Virchow, it is not rare to find in lipomata isolated cavities the contents of which are partly fluid and partly saponified. Saponifying necrosis of lipomata has been reported by a number of observers ("soap cysts," "butter cysts"). The necrotic areas appear whitish, opaque, and of a cheesy consistence. Lime salts may be deposited in such necrotic areas, and in this way there may be formed calcareous nodules throughout the growth. A deposit of lime salts may occur also within the stroma of the tumor. In some cases the entire growth may become calcified. Ossification has also been reported as occurring within lipomata. Liquefaction of portions of the fat tissue may occur. Through the rupture and confluence of fat cells pseudocysts filled with oil may be formed (oil cysts). The twisting of the pedicle of a polypoid lipoma may lead to the necrosis and sloughing of the entire tumor. Self-healing may result in this way. In some cases a serous atrophy of the fat tissue takes place, the tumor assuming the character of an œdema and partial liquefaction of the fat tissue. The fat may be removed from the cells and the lipoma changed into a fibroma. Myxomatous degeneration converts the tumor into a myxolipoma. This is the most common retrograde change occurring in fatty tumors; and is of the nature of a metaplasia. Retrograde changes are most common in the lipomata of the skin, since in this location the tumors are most exposed to injury and to the possibility of infection.

Diagnosis.—The nature of the gross appearances, the clinical history, etc., make the diagnosis easy in those cases in which the tumor can be seen and directly palpated. The subcutaneous lipomata are slowly growing, lobulated, movable tumors, and give pseudofluctuation. In the case of large lipomata of the internal organs the negative results of aspiration in the case of a fluctuating tumor would lead to the suspicion of lipoma, particularly in the case of retroperitoneal tumors. The presence of inflammatory changes and the development of cachexia are suggestive of sarcomatous change. Neuralgic pains may be associated with lipomata. The symptoms in general are dependent upon the position and size. Lipomata of internal organs may give rise to important pressure symptoms. In the great majority of cases, however, the only effect is a cosmetic one. In spite of the great size to which they frequently attain lipomata do not usually influence the general metabolism of the body.

Prognosis.—The prognosis in lipoma is favorable. Since this form of tumor produces no metastases it must be classed with the benign neoplasms. Sarcoma may develop in a lipoma, but this occurrence is very rare, more so than in the case of any other of the benign connective-tissue tumors. Sarcomatous change appears to be more common in the case of tumors containing both adipose and myxomatous tissue (myxolipoma), the resulting sarcoma being of the nature of a myxosarcoma. This change occurs most frequently in lipomata of the intermuscular connective tissue. The cases reported in the literature as metastatic lipomata are undoubtedly examples of sarcomata containing fat tissue. No evidence exists of the metastasis of a pure lipoma. As a rule, the growth of a lipoma is gradual and slow, with periods of apparent quiescence. In the case of infected lipomata, particularly those of the skin, the prognosis is more grave, since the conditions favor the occurrence of phlegmonous inflammations with resulting septicæmia or pyæmia. Such complications are, however, on the whole rare. In the case of large lipomata of internal organs the prognosis depends upon the location of the growth, the extent of the pressure symptoms, the organs thus involved, etc. The removal of a lipoma usually results in a cure, recurrence being very rare.

Treatment.—The treatment is purely surgical. In the case of subcutaneous lipomata local anæsthesia is usually sufficient. It should be borne in mind that the capsule should be removed in all cases of lipoma, since very often the new formation of fat tissue proceeds from the fibrous capsule. In the case of the diffuse forms the prolongations of fatty and fibrous tissue extending into the surrounding tissues should be dissected out, as from these a recurrence may take place. In those cases in which the tumors are covered by atrophic or inflamed skin the incision is best made at the base of the growth and not over it. Tearing should be carefully avoided. Drainage is not necessary. The strictest aseptic precautions should be observed during the operation and afterward, since the condition of the tissues about the growth favors infection and the occurrence of phlegmonous inflammations. *Aldred Scott Warthin.*

LIVER, TUBERCULOSIS OF THE.—Without exception all writers agree as to the rarity of primary tuberculosis of the liver, a number going so far as to affirm that an undoubted case of primary hepatic tuberculosis has not yet been reported. Such an apparent immunity on the part of this organ to tuberculous infection cannot be explained by any lessened opportunities for infection, as compared to other organs, such as the kidneys, testicles, etc., in which a primary tuberculosis of clinical importance is not so rare. Indeed, it would appear that the liver with its large extent of vascular surface and the relatively slow circulation in its blood spaces would stand a very good chance of infection from tubercle bacilli that have gained a cryptogenic entrance into the blood stream. Further, the fact that tubercle bacilli may be taken into the alimentary canal in the food and drink would lead to the supposition that the portal veins would constitute one of the avenues of tuberculous infection. These considerations would make it seem probable that primary hepatic tuberculosis would occur more often than we actually find to be the case. It is the opinion of the writer that small healed primary tubercles not infrequently occur in the liver. As is well known to every pathologist, small nodules of hyaline connective tissue varying in size from that of a pinhead to that of a pea are not rare in this organ. By the majority of writers they have been regarded as small fibromata or healed gummata. The fact that some of these little nodules consist of a caseous centre surrounded by a connective-tissue capsule, and that others present an earlier stage of caseating epithelioid tissue with beginning encapsulation, has led the writer to regard the majority of such nodules as healed tubercles. Similar small fibroid nodules are also

frequently seen in the spleen and kidneys and are similarly interpreted. If the probabilities of infection, the not infrequent occurrence of healed tubercles, and the extreme rarity of primary hepatic tuberculosis of clinical importance be considered, it would seem that the liver possessed a relatively high resistance to tuberculosis.

Such a relative immunity undoubtedly exists in the fœtal liver. A number of cases have been reported of maternal tuberculosis in which the liver of the fœtus contained great numbers of tubercle bacilli (as shown by staining and animal inoculation) without histological lesions of tuberculosis. Such a case has recently been reported by the writer. The seven-months fœtus of a woman dying from acute miliary tuberculosis was examined carefully for evidences of congenital tuberculosis. The placenta presented a marked miliary tuberculosis. Tubercle bacilli were found in the hepatic vessels of the fœtus, and the inoculation of a guinea-pig with an emulsion of fœtal liver gave positive results. Agglutination thrombi were found in the liver capillaries, but no histological evidences of tuberculosis. Several cases, however, have been reported of probable congenital tuberculosis in which tuberculous lesions were found in the liver, the infection being regarded as taking place through the umbilical vein from the placenta. These cases are therefore to be classed as primary hepatic tuberculosis.

If primary tuberculosis of the liver is rare, secondary involvement of this organ is one of the most common pathological findings. Not only in cases of acute miliary tuberculosis are great numbers of tubercles found in this organ, but also in all advanced cases of chronic pulmonary and bone tuberculosis. Even in cases in which the disease of the lung is not very extensive scattered secondary tubercles may be found throughout the liver. As a rule, these secondary tubercles are very small, and as it is rarely possible to recognize them by the naked eye at autopsy, they are frequently overlooked. In the great majority of cases their presence can be demonstrated only by microscopical examination. The larger ones (size of a mustard seed to that of a pea) are grayish, semitranslucent, with yellowish opaque centres. They can be best seen in the livers of children where they often are several millimetres in diameter. The infection is usually hæmatogenous, and the microscopical picture presented is that of a disseminated miliary tuberculosis of the organ. Occasionally larger caseous nodules are found in connection with miliary tubercles, and more rarely tuberculous cavities or abscesses. Still more rarely there are found large solid caseous nodules in the liver resembling the solitary tubercles of the brain. These may be mistaken for cancer nodules or gummata. Such large nodules may not show any especial connection with the bile ducts, and it is probable that in some cases they represent primary tubercles.

The number of the miliary tubercles may be so great that each section may be full of them; in other cases it may be necessary to examine many sections before a tubercle is found. In the case of pulmonary and bone tuberculosis and general miliary tuberculosis the infection of the liver is usually through the hepatic artery; in the case of intestinal tuberculosis it may take place through the portal vein or lymphatics. The tubercles, in infection either through the hepatic artery or through the portal vein, are found chiefly at the periphery of the lobule and in the interlobular connective tissue. A small number may be found in the intermediate and central zones of the lobule. As the nodules increase in size they extend in from the periphery and cause a destruction of the liver cells.

The writer believes that in the great majority of cases the earliest step in the formation of a liver tubercle is an agglutination thrombosis in the liver capillary. The deposit and growth of tubercle bacilli upon the endothelium of the capillary wall and the consequent injury to the endothelial cells are probably chiefly responsible for this thrombosis. As a result of the thrombosis and of the injury to the endothelium, as well as from the formation of toxins, the neighboring liver cells undergo degeneration or necrosis. There is a collection of leucocytes at the affected point, and these may also undergo necrosis. Following the degenerative changes there is a proliferation of the endothelium and of the neighboring connective tissue leading to the formation of an epithelioid tubercle which sooner or later shows a central caseation. The smallest tubercles may show no inflammatory reaction about them. Giant cells may be present in large or small numbers, or may be entirely absent. They arise from the proliferating endothelial and connective-tissue cells, and possibly also from the leucocytes. As the nodules increase in size they may become confluent. As the result of an interstitial infiltration about the tubercles the picture of a diffuse cirrhosis may be presented, newly formed connective tissue being found not only between the lobules, but also growing into the latter. The greater the number of tubercles the closer the resemblance to a cirrhosis. An increase of the small bile ducts may be observed in the neighborhood of the tubercles. A true atrophic cirrhosis may result, but usually death occurs before this condition has time to develop. It should be remembered also that the tuberculosis may occur secondarily in a cirrhotic liver.

In very acute cases of general miliary tuberculosis with a high degree of virulence the only lesions found in the liver may be areas of focal necrosis of the liver cells. These areas may be so large as to be easily seen with the naked eye. The blood spaces of the necrotic areas are filled with fibrin and agglutinated red cells. Large colonies of tubercle bacilli may be found in the necrotic foci. No proliferation of the endothelium or connective tissue may be present; giant cells are entirely absent. The process can be recognized as tuberculosis only by staining for tubercle bacilli. The writer has seen two cases of this kind which were diagnosed as typhoid fever; the autopsy showed large focal necroses in liver, spleen, and kidneys, those in the liver and spleen being most numerous and largest. No epithelioid proliferation or giant cells were found about these areas, and the tuberculous nature of the process was recognized only on staining for tubercle bacilli, when each caseous focus was found to contain great numbers of the latter. In general miliary tuberculosis of a less virulent type small focal necroses of this kind are also found in association with epithelioid, lymphoid, and caseating tubercles. It is also to be noted that in such cases the lesions in the liver are usually smaller than in other organs, and this fact may also be taken as an indication of a greater resisting power on the part of the liver to tuberculosis.

In the case of hepatic tubercles occurring secondarily to chronic tuberculosis of other organs the liver may show such changes as amyloid and fatty infiltration. The latter change is practically always present. In chronic pulmonary tuberculosis the liver shows usually a more or less marked chronic passive congestion (nutmeg liver). In acute miliary infections the liver cells show cloudy swelling, fatty degeneration, or simple necrosis.

Hanot and Gilbert distinguish the following forms of hepatic tuberculosis:

1. Acute hépatite tuberculeuse graisseuse hypertrophique.

2. Subacute. (*a*) Hépatite tuberculeuse graisseuse atrophique ou sans hypertrophie; (*b*) hépatite tuberculeuse parenchymateuse nodulaire.

3. Chronic. (*a*) Cirrhose tuberculeuse; (*b*) foie gras tuberculeux (without tubercles).

A rare complication of hepatic tuberculosis is secondary carcinoma of this organ. Several cases of this kind have been reported, and the writer has seen a similar case in which both the tuberculous infection and the metastasis of the carcinoma were through the portal vein.

More rare than secondary miliary tubercles of the liver are larger caseous nodules, the centres of which contain cavities filled with bile-stained caseous material. These cavities may be of the size of a walnut. The process represents a tuberculosis of the bile ducts, the walls of which become caseous. The infection is probably

lymphogenous, and has the character of a tuberculous periangiocholitis. In very rare cases the infection may take place through the bile ducts themselves. In the great majority of these cases, however, the tuberculous process begins around the bile duct and invades its mucosa only secondarily. Hæmatogenous hepatic tubercles may or may not be associated with this condition.

The liver and the peritoneum may be involved at the same time, but this organ is rarely involved from the latter or from the omentum.

In experimental hepatic tuberculosis in animals the process runs a more acute course, being characterized by larger areas of necrosis.

The clinical symptoms of hepatic tuberculosis are slight, and the condition can but rarely be distinguished from the miliary or chronic process with which it is associated. The occurrence of icterus or the rapid development of a painless ascites points to the development of tuberculosis of this organ. In children the organ may become enlarged and sensitive. *Aldred Scott Warthin.*

MICTURITION, DISORDERS OF.—Given normal urine and a normal genito-urinary tract, micturition is accompanied and followed by no other sensation than one of relief, and is performed normally from four to twelve times in twenty-four hours, depending upon the temperature and humidity of the air, the amount of exercise taken, the intensity of the mental occupation and the degree of anxiety which it entails, the volume of water drunk, and—to a less extent—upon the kind of food ingested.

Many of the disorders of micturition are directly augmented or exaggerated by excessive acidity of the urine on the one hand, or excessive alkalinity on the other; a few of the disorders are directly caused by these conditions.

With rare exceptions the several disorders are interdependent and correlative. No one disorder may be said to occur alone.

For convenience in reference, the disorders of micturition are given alphabetically; but the several possible causes of each disorder are arranged as nearly as possible according to the relative frequency of their clinical occurrence.

Diminished Stream.—This disorder may be either (1) temporary, or (2) constant until relieved by surgical intervention.

1. When temporary or of short duration a diminution in the size of the stream points to a transient obstruction, *e.g.*, congestion at some point or zone in the urethra or a urethral spasm.

As a result of inflammation, any part of the urethral canal may become swollen to the extent of obstructing the urinary stream to a greater or less extent. Thus we may have a diminished stream due to a severe acute urethritis affecting the anterior urethra, with or without involvement of the posterior urethra. It may also be observed in connection with an acute prostatitis.

Any lesion of the urethra—*e.g.*, organic stricture, especially if irritable, or a granular patch—is capable of exciting urethral spasm, especially in neurotic individuals. The diagnosis must be made partly by exclusion, but chiefly by exploration of the urethra with a bougie-à-boule, sound, and endoscope.

2. A diminished stream which either shows no tendency to grow larger or undergoes a progressive further diminution in size, points to an organic obstruction. In all cases of this nature of long standing the resulting atony of the bladder plays an important though secondary part in the character of the stream.

Organic stricture, when neglected, gives a stream which tends constantly but slowly to diminish in size. If the stricture be situated at or near the meatus the stream will be small and scattering, but forcible; if it be situated deeper within the canal, the forcible projection will be lacking. When the stricture becomes inflamed from any cause, the diminution progresses rapidly and may persist until complete retention results.

Prostatic enlargement has among its early symptoms a diminution of the urinary stream. As micturition begins, the stream is small and feeble, sometimes dribbling; it then becomes larger and, except in the later stages of enlargement of the prostate, attains a fair volume and force, only to become again small and feeble and usually dribbling as the act is completed.

Chronic contraction of the prostatic fibres surrounding the neck of the bladder gives the same symptoms as does commencing enlargement of the prostate. In the differential diagnosis the chief point is the age of the patient; in many cases the diagnosis cannot be made without an exploratory perineal section.

Periurethral abscess may cause a narrowing of the urethra and thus diminish the stream; when situated in the bulbous portion the abscess may cause acute retention.

A partial plugging of the urethra by a small calculus arrested on its way from the bladder produces a diminution of the stream that becomes more marked as inflammatory congestion advances. If the calculus is rough there will follow an oozing of blood from the meatus, unless the urethral mucous membrane happens to be deeply cicatricial at the point of arrest. Palpation along the course of the urethra—per rectum for the posterior portion—rarely fails to detect the calculus. Instrumental exploration usually is conclusive.

A partial plugging of the outlet of the bladder by a pedunculate tumor or a small movable calculus will give rise to a diminished stream accompanied by symptoms more or less pathognomonic of the lesion present. The diagnosis is materially aided by the fact that immediate relief is obtained by dorsal decubitus or by the dislodgement of the obstruction by means of a sound or searcher.

Urethral polypi diminish the stream in proportion to their size. When they are very small there may be no symptom except hemorrhage.

Dribbling.—In addition to the dribbling that characterizes the first and second forms of incontinence, and which is sufficiently described in subsequent paragraphs, still other types of dribbling may be recognized. Thus we have:

1. The involuntary, painless escape of a few drops of urine at the end of micturition.

2. The voluntary, not always painless, escape of a few drops of urine at the beginning of micturition.

3. The urine is voided in drops throughout micturition.

(1) In prostatic enlargement the dribbling of a few drops of urine at the end of micturition is a common and early symptom. It is independent of the degree of vesical atony which may be present; in fact, it may exist without the presence of any vesical atony whatever.

In chronic urethritis (anterior or posterior or both) the dribbling, when present, is constant until the muscular tone of the urethra has been restored.

In stricture of the urethra of large calibre the final drops of urine are caught behind the stricture and dribble out into the clothing.

In chronic contraction of the prostatic fibres surrounding the neck of the bladder the dribbling at first is an intermittent symptom; later, it is constant.

(2) In prostatic enlargement the voluntary and not always painless escape of a few drops of urine occurs at the beginning of micturition. It is preceded by hesitancy and gradually gives way to the full stream, which in turn dies away and ends with dribbling.

(3) In filiform stricture of the urethra, if it has existed for a relatively short period of time, and consequently is associated with only slight atony of the bladder, the stream is of a dribbling character, and is produced with more or less effort.

In acute prostatitis (including prostatic abscess) and in acute seminal vesiculitis the urine is voided in drops when retention threatens, either from mechanical obstruction or as the result of reflex irritation.

Frequency and Urgency; Pain and Tenesmus.—Frequency of urination may be normal, or physiologic, within wide limits. It is abnormal, or pathologic, when

accompanied by urgency, pain or tenesmus, or when due to a tangible, pathologic condition or to that obscure pathologic state called a neurosis. Frequency rarely occurs without at least a trace of urgency; frequency and urgency are practically never without a degree of initial or terminal pain and tenesmus. Frequency due to quantity alone is not included, it being dependent, strictly speaking, upon a disorder of elimination.

In acute posterior urethritis, when this is severe, frequency and urgency are marked; a lesser grade gives only frequency; the mildest grade of all does not occasion any disorder of micturition. In every case of acute posterior urethritis a digital rectal examination should be made to ascertain whether acute prostatitis and acute seminal vesiculitis are present.

In chronic posterior urethritis there is, in most cases, a very trifling frequency which shows a tendency to increase and may become complicated by urgency, as well as occasionally by pain and tenesmus, during an exacerbation of the local congestion. In a few cases frequency is constant, and is accompanied by more or less urgency and slight initial and terminal pain, with very moderate tenesmus.

In organic urethral stricture the frequency is due to the maintenance of a chronic posterior urethritis. Usually it is diurnal only. Later on, chronic partial retention is added, and, the symptoms becoming exaggerated by the congestion due to this retention, urgency and possibly pain and tenesmus develop.

In acute prostatitis and acute seminal vesiculitis (including prostatic abscess) there may be, in the early stage, simply increased frequency, but usually both this symptom and urgency coexist from the outset, and with them are associated more or less pain and tenesmus. Very rarely there is no disorder of micturition. Digital rectal examination affords the only means of establishing the diagnosis.

In chronic prostatitis and chronic seminal vesiculitis a slight, uncomplicated, diurnal increase in frequency is a characteristic of the disease. It tends to increase and urgency develops during the occasional mild exacerbations to which the coincident posterior urethritis is liable.

In prostatic enlargement, uncomplicated increase in frequency, especially if nocturnal, in a man forty-five years of age or older, who gives no history of a previous increase in frequency, is pathognomonic of the early stages of this affection. The frequency increases with the enlargement, and sooner or later becomes diurnal as well. Still later it becomes complicated by urgency and pain, and then by tenesmus, all of these depending upon the degree of prostatitis and urethrocystitis that have developed, and in some cases (especially those of an advanced type) upon the presence or absence of a calculus.

All varieties of acute cystitis cause increased frequency of micturition. If the inflammation be severe, or if it centre about the neck of the bladder, as it commonly does, there will be extreme frequency with urgency, which latter symptom may amount to a slight incontinence on occasions. There will also be pain and tenesmus, the latter sometimes amounting to strangury. As a rule, however temporary relief quickly follows the terminal pain and tenesmus.

In chronic cystitis frequency of micturition may be absent during the quiescent periods and during mild exacerbations. Urgency is rare. Unusual frequency with urgency, pain and tenesmus, denotes a sharp exacerbation. Oft-recurring exacerbations in cases with little or no prostatic enlargement furnish strong presumptive proof of the presence of a calculus in the bladder; and when such exacerbations occur in cases in which the prostate is enlarged, they indicate either that a fresh infection has taken place, or that there is a calculus in the bladder, or both. When a sharp hæmaturia accompanies the exacerbations a differential diagnosis will be required between ulceration—simple, gonorrhœal, or tuberculous,—a calculus, and a neoplasm.

When a calculus is present in the bladder, diurnal rather than nocturnal increase of frequency is a characteristic of the condition. Micturition is usually accompanied by pain, sometimes also by tenesmus, depending upon the size of the calculus, the character of its surface, and the degree of cystitis. Thus the increased frequency may become practically incontinence. The terminal pain is referred usually to a point about an inch back from the meatus. When the calculus is small and mobile, and therefore capable of rolling against the vesical outlet, there occur sudden attacks of increased frequency, urgency, pain and tenesmus, with a minimum of cystitis. Recumbency lessens the suffering; occasionally it gives complete relief. Exercise, especially that which jolts the pelvis, aggravates the symptoms.

In pyelitis, when acute and of high grade, the frequency, urgency, pain, and tenesmus referred to the neck of the bladder, may simulate vesical calculus. Chronic pyelitis gives at most a slight increase in frequency of micturition.

The presence of a small tumor in the bladder, if it be seated at a point remote from the outlet, may not affect micturition. In a case of this character an uncomplicated hæmaturia is the only symptom that would point to the presence of the tumor. Larger tumors produce increased frequency which is in direct proportion to their size; they also produce urgency, pain, and tenesmus, all of which symptoms depend for their severity upon the location and mobility of the tumors. This applies also to polypi in the prostatic urethra.

In ulcer of the bladder, simple, gonorrhœal or tuberculous, urgency depends upon the proximity of the ulcer to the vesical neck. If it be situated within the neck, there will be more or less pain and tenesmus, sometimes initial as well as terminal, with more or less hæmaturia.

In vesical tuberculosis an otherwise unaccountable increase in frequency, diurnal and nocturnal, is an early symptom. Cystoscopy often aids in the diagnosis. Later, the presence of urgency, pain, and tenesmus, and their severity, depend upon the proximity of the lesion to the vesical neck and upon the extent of the lesion independently of its location. In advanced cases the pain and tenesmus usually are very severe and may be accompanied by hæmaturia. A negative examination for tubercle bacilli in the urine is not conclusive.

In renal tuberculosis, renal calculus, and ureteral calculus, when not complicated by cystitis, these affections may give rise to an uncomplicated diurnal increase in frequency. Renal colic, due to any one of the above causes or to movable kidney, may be accompanied by reflex increase in frequency, urgency, pain, and tenesmus.

Among the acute symptoms associated with intermittent hydronephrosis there is usually more or less increase in frequency of micturition, often accompanied by urgency, pain, and tenesmus; the severity of these symptoms depending upon the cause of the hydronephrosis. As the attack subsides and the pent-up urine is liberated, there is likely to be a slight, uncomplicated, transient increase in frequency due to the sudden increase in the quantity of the urine.

In tuberculous prostatitis the incipient stage and occasionally a more advanced stage give, as a rule, no urinary symptoms. When the disease is well advanced it causes increased frequency and more or less urgency, accompanied by terminal pain and tenesmus so sharp as to simulate vesical calculus. The diagnosis is established by exclusion and by the discovery of nodules in the prostate on digital rectal examination. A negative examination for tubercle bacilli in the urine is not conclusive.

Increase in frequency of micturition occurs as a neurosis in young and neurotic individuals, and possibly also in neurasthenic men. The increased frequency is diurnal and may become exaggerated by the large quantity of urine which these patients sometimes excrete. In some cases any attempt to postpone the act of micturition causes severe pain. The differential diagnosis between this neurosis and incipient vesical tuberculosis is sometimes difficult without the aid of cystoscopy.

In hernia of the bladder, before cystitis has developed, increase in frequency is the only urinary symptom. The pathognomonic signs are a more or less tense, fluctuating tumor in the usual site of an inguinal hernia; its disappearance under gentle manipulation while the patient is recumbent; his ability to rise and void another volume of urine, although he emptied his bladder immediately before the reduction; and, finally, the reappearance of the tumor when the bladder is distended with fluid.

In contracted bladder the increase in frequency is as pronounced during the night as it is during the daytime. When the contraction is due to interstitial changes following long-standing chronic cystitis from any cause, or when it is due to advanced tuberculosis, progressive or stationary, there are increased frequency, some urgency, and more or less terminal pain and tenesmus.

Two very rare conditions—a congenitally small bladder and an undeveloped bladder due to a long-neglected incontinence in childhood that has resulted in the habit of frequent micturition—give equal diurnal and nocturnal increase in frequency as the only symptoms so long as there are no complications.

In chronic lesions of the spinal cord, a degree of increased frequency, which may well be described as an irritability of the bladder, is common in the earliest stages. Later on, there occurs an increase in frequency which is dependent upon distention of the bladder.

Hesitancy or Slowness in Starting the Stream.—As a pure neurosis hesitancy is very common; it is seen in the difficulty which certain patients experience when they attempt to urinate in a hurry or in the presence of others.

In prostatic enlargement hesitancy is an early and practically constant symptom. In chronic contraction of the prostatic fibres surrounding the neck of the bladder it is equally common.

In acute inflammatory conditions of the urethra hesitancy is due either to urethral spasm as such, or to an inhibitory effect through fear of the *ardor urinæ*.

Chronic lesions of the urethra—*e.g.*, granulations or an irritable stricture—sometimes produce a momentary urethral spasm.

In acute and chronic inflammatory affections of the prostate and seminal vesicles hesitancy may result either from the slight mechanical obstruction offered or from a slight urethral spasm.

Painful diseases of the rectum—*e.g.*, ulcer, fissure, or inflamed hemorrhoids—not infrequently produce a momentary urethral spasm.

Incontinence.—Three forms are recognized: 1. A constant, passive, more or less continuous flowing away of the urine. 2. An involuntary escape of a few drops of urine on occasions. 3. An inability to retain sufficient urine in the bladder to constitute an act of micturition, or the constant voluntary—sometimes involuntary—emptying of the bladder by the expulsion of a few drops very frequently. (The nocturnal enuresis of children is not included, as it does not come properly under the title of this article. See *Enuresis*.)

1. This first form is true incontinence. Ordinarily it occurs under only two conditions: (*a*) overdistention of an atrophic bladder; (*b*) atony of the vesical sphincters, with or without atrophy.

Prostatic enlargement is the most classic cause of overdistention with atrophy and therefore of true incontinence in a man past the age of fifty-five. The incontinence is chiefly, if not wholly, nocturnal. Filiform stricture of the urethra, if of long standing and associated with marked atony of the bladder, bears the same relation to true incontinence in younger men. Here the incontinence is chiefly diurnal, and often alternates with acute retention.

Among the diseases of the spinal cord locomotor ataxia (tabes dorsalis) and other scleroses often cause atony of the bladder, thus permitting overdistention and true incontinence. Spastic contractions of the vesical sphincters will foster the overdistention; sensory disturbances causing anæsthesia of the region will augment the incontinence. On the other hand, the reverse—viz., atony of the sphincters and hyperæsthesia—may obtain.

2. This form of incontinence presents many grades and is a symptom of several different lesions. The occasions on which it occurs are: exacerbations in the causative lesions, and any sudden unusual pressure upon the bladder, such as takes place in coughing, sneezing, jumping, or lifting a weight. The causative lesions are: chronic posterior urethritis; ulcers near the neck of the bladder, simple, gonorrhœal, or tuberculous; vesical calculi; vesical tuberculosis, especially when affecting the neck, whether with or without ulceration; renal tuberculosis ("slight incontinence with frequency, in the absence of other lesions, is strongly suspicious of renal tuberculsis"); contracted bladder due to antecedent extreme pericystitis or interstitial cystitis; chronic prostatitis; slight atony, or "relaxation," of the vesical sphincters without atony of the bladder.

3. This is the least characteristic form of incontinence. It is merely an extreme frequency with uncontrollable urgency, and is therefore complicated by more or less pain and tenesmus. The lesions that cause it are: severe acute posterior urethritis; acute cystitis; a large rough, movable calculus, or a collection of facetted calculi, occupying the cavity of the bladder and partially distending it; a small, rough calculus, lodged in the prostatic urethra; renal calculi, causing attacks of severe colic.

Interrupted Stream.—This is also known as the "stammering stream."

The causes of this disorder operate either (1) mechanically, by intermittent obstruction, or (2) reflexly, by intermittent excitation of the vesical sphincter. Under the first class are: Prostatic enlargement; chronic contraction of the prostatic fibres surrounding the neck of the bladder; a small, rounded, mobile calculus; a pedunculate tumor; a blood clot. Under the second class are: Acute, subacute, and chronic urethritis; stricture of the urethra, both of large and small calibre; neurasthenia and neurotic tendencies.

Retention.—Confusion arises from the use of the word retention when suppression is meant. Retention of urine applies only to its discharge from the bladder, while suppression of urine applies only to its excretion by the kidneys.

Retention is due either to a mechanical obstruction, which prevents the escape of urine from the bladder, or to a diminished expulsive power on the part of this organ; this latter condition being due in turn to impaired innervation of the muscle coat, or possibly to some actual lesion of the muscle. In obstructions of long standing the retention is due to a combination of both these factors, for the hypertrophy which developed in the wall of the bladder as a result of its early efforts to overcome the obstruction finally gives way to an atrophy, the degree of which is in direct ratio to the chronicity of the obstruction.

I. Acute Retention.—The cause may be (*a*) organic obstruction; (*b*) spasmodic obstruction; (*c*) a combination of both; (*d*) a sudden impairment of the bladder function, with or without spasm of the sphincter.

(*a*) The following are among the more important organic obstructions: a stricture of small calibre, when inflamed by sexual and alcoholic excesses, by excessive coffee drinking, or by exposure to cold and wet; a prostatic enlargement, when acutely congested or inflamed—a condition to which it is peculiarly liable after any excesses in venery, eating, and drinking, and as a result of constipation; acute prostatitis, simple or gonorrhœal, especially when resulting in an abscess that is pointing toward the bladder; a rupture of the urethra, complete or partial; plugging of the internal meatus, *e.g.*, by a small, movable calculus, a pedunculate vesical tumor, or a blood clot; and, finally, periurethral abscess, especially when located in the bulbous portion. Among the rare organic obstructions should be mentioned: Acute posterior urethritis, severe acute seminal vesiculitis, tuberculous prostatitis, and papilloma of the urethra.

(*b*) Spasmodic obstruction—*i.e.*, obstruction caused

by spasm of the sphincter—occurs under the following circumstances: in acute anterior urethritis, occurring either independently or in connection with an existing urethral lesion (*e.g.*, a stricture or a granular patch); when the urethra is the seat of a comparatively slight trauma, inflicted by a blow, by rough instrumentation, or by irritating injections; when there are rectal lesions, including fæcal impaction and even constipation of only two or three days' standing; after operations, minor as well as major, on the urethra or on the rectum or some contiguous region, whether performed under local, spinal, or general anæsthesia; in the presence of shock, post-operative or traumatic; as a result of enforced postponement of micturition, especially if there is present any lesion of the urethra, prostate, or seminal vesicles;* in exhausting diseases, such as typhoid fever, pneumonia, peritonitis, and meningitis; in vesical tuberculosis; in pyelitis, simple, gonorrhœal, tuberculous, or due to a calculus (the last-named occasionally causes acute retention instead of the more usual frequency and urgency of micturition); in hernia of the bladder—a rare occurrence; and, finally, in neuroses and neurotic conditions in general.

(*c*) A combination of organic and spasmodic obstructions is observed in severe acute posterior urethritis, when the swelling is extreme and when spasm is excited. It is also observed in severe acute prostatitis and in seminal vesiculitis.

(*d*) Sudden impairment of the bladder function, with or without spasm of the sphincter, may be observed in rupture of the bladder, whether intra- or extraperitoneal, and also in those injuries or diseases of the central nervous system which result in the production of a sudden hemiplegia or paraplegia, with or without coma.

II. Chronic Retention.—This is either partial or complete. Chronic partial retention results when only a portion of the urine is spontaneously voided, the rest remaining in the bladder as "residual urine." Chronic complete retention exists when all spontaneous micturition has been lost and all the urine has to be drawn by catheter.

In prostatic enlargement there is at first only partial retention. This advances to complete retention if, the true state of affairs not being recognized, the bladder is allowed to become atonic through overdistention. Thus arise the cases of chronic complete retention which have apparently assumed this character from the outset. An intercurrent acute retention is often the first symptom for which the patient seeks advice, he having disregarded the symptoms of the partial retention.

The remarks made in reference to prostatic enlargement in a preceding paragraph apply with equal appropriateness to chronic contraction of the fibres surrounding the neck of the bladder. This chronic contraction, however, is less frequent than prostatic enlargement, and consequently it gives rise less often to chronic complete retention.

In filiform stricture of the urethra the chronic retention is only partial; it will disappear after appropriate treatment of the stricture unless the latter has been neglected for many years.

In chronic prostatitis, in tuberculosis of the prostate, and in vesical tuberculosis a small quantity of residual urine is an almost constant objective symptom.

As further causes of chronic retention may be mentioned: habitual failure to empty the bladder completely by reason of hurry or indifference; and frequently repeated prolonged postponement of micturition, thus causing frequent overdistention.

While the retention which originates in some chronic lesion of the spinal cord is only partial, it is nevertheless characterized by a large volume of residual urine—from five to twenty ounces. In the mild cases the amount of the residual urine will fluctuate even under the best conditions, often falling to two ounces. On the other hand, the amount is fairly constant in the more advanced cases, and the retention is associated with frequency, or with incontinence, or with both. *James Pedersen.*

* In these cases the spasm is usually of short duration, and it is rarely found necessary to resort to the use of the catheter in order to secure relief for the patient.

MOUTH, DISEASES AND INJURIES OF.—I. Stomatitis.—"This word, which from its derivation signifies inflammation of the mouth, is held to include inflammatory affections of the cavity of the mouth as far back as the soft palate. Any abnormal condition of an inflammatory character which involves the gums, the tongue, or the inner surface of the cheeks, is included, therefore, under the designation of stomatitis. Experience shows that there is little tendency toward limitation to any one of these structures—usually the entire cavity of the mouth partakes of the diseased condition.

"The affections included under this name are, in great part, limited to the age of childhood. Adults are never the subjects of certain forms of the disease, and seldom suffer from any variety of it, save as part of some other morbid condition. Not infrequently, however, stomatitis is nothing more than a part of such general condition. Diphtheria sometimes involves the mouth as well as the tonsils, pharynx, and palate; inflammation, with pustulation in the mouth, may occur in smallpox, varioloid, and varicella; facial erysipelas often presents an inflamed condition of the mouth; measles, Rötheln, and syphilis are accompanied by characteristic mouth affections; and many drugs, such as mercury and iodine, in addition to the mineral and other stronger acids, produce an abnormal condition." (From former edition of Reference Handbook.)

It must be remembered that in children there is a tendency to put anything and everything—all germ-laden—into the mouth; hence one reason why stomatitis is so much more common at that age. The troubles incident to the period of dentition have also a causal relation to stomatitis.

As remedies for stomatitis in general, the following have been used. As mouth washes, in the form of solutions: Potassium permanganate, gr. ij. to ℥i.; potassium chlorate, gr. x.–xx. to ℥i.; boric acid, saturated solution; carbolic acid, one-per-cent. solution; hydrogen dioxide, 15 vols. per cent.; silver nitrate, gr. x.–xx. to ℥i. Also the solid stick of silver nitrate may be employed; and potassium chlorate may be given internally in doses of gr. v.–viij. q. 4 h.; in the case of children, however, the latter remedy must be used with care. Tonics of iron, quinine, nux vomica, and cod-liver oil are required. The diet must be liquid, either warm or cold, and must be generous and sufficient; chipped ice and iced water are acceptable to the patient. The mouth must be regularly washed or, if that is not possible, sprayed. If the gums are spongy, they should be painted with tincture of myrrh.

2. Catarrhal Stomatitis.—(*Synonyms:* Acute stomatitis, Erythematous stomatitis, Pultaceous stomatitis, Simple stomatitis, Superficial stomatitis.)

Etiology.—It most commonly occurs in infants and children, but it is also found in adults. The most common cause is an irritant either chemical or mechanical, such as overheated or too highly spiced food, acids, alkalies, very hot beverages, broken or carious teeth, and the excessive use of tobacco or alcoholic drinks. In the case of infants irritation caused by a coral, by difficult dentition, by a poorly developed or unclean nipple, or by a feeding bottle which has not been properly cleansed, may produce stomatitis. An excess of sugar or starchy food, and also exposure to cold, are causative factors in some cases.

Symptoms.—These are the classical symptoms of inflammation: redness, first in patches, later more general; swelling, chiefly of lips, cheeks, gums, and tongue, the latter often showing the impression of the teeth; disordered secretion—in the adult the mouth is at first dry, later there is an increased flow of saliva with secretion of considerable mucus; at the same time the breath is fetid, and in children there is dribbling accompanied with considerable tenderness, so that the infant refuses to nurse or

to allow the mouth to be cleansed. In adults the pain is as a rule slight, though it may be considerable, and, in conjunction with the dryness of the mouth seen in the early stages, renders mastication difficult. The disorder usually lasts about a week. In this form of stomatitis there is no ulceration.

Prognosis is good in acute cases, but infants are liable to suffer from inanition owing to the pain experienced in taking food. In chronic cases, generally due to alcohol or tobacco, the offending substance must be withdrawn.

Treatment is chiefly hygienic; whenever possible the causes must be removed and strict cleanliness insisted upon. In mild cases mouth washes of borax, of potassium chlorate, or of sodium bicarbonate may be useful; in the severer forms silver nitrate in one-per-cent. solution should be applied. At the same time general treatment in the shape of tonics and salines must not be overlooked. In infants the feeding apparatus must be kept scrupulously clean.

3. Croupous or Membranous Stomatitis is an inflammation of the mouth with the formation of a false membrane of a yellowish-white or grayish-white color. The disease may be diphtheritic or it may be due to gonorrhœa or syphilis; it is also caused by extremes of temperature (as frost-bite) and by chemical irritants. This form of stomatitis is much the same as diphtheria, but without the Klebs-Loeffler bacillus. The pseudo-membrane is apt to ulcerate and become detached from the subjacent tissue which then shows marks of erosion.

Treatment.—If the inflammation is due to diphtheria, give antitoxin; in most other cases the treatment is the same as in other forms of stomatitis, and consists of good food, proper hygiene, antiseptic and astringent mouth washes, tonics, and stimulants.

4. Ulcerative Stomatitis.—(*Synonyms:* Fetid stomatitis, Phlegmonous stomatitis, Stomacace, Putrid sore mouth, Phagedenic gingivitis.)

This form of stomatitis is a serious condition in which there is a superficial necrosis of the mucous membrane of the mouth, with subsequent ulceration.

Etiology.—The disease is probably caused by a microorganism, though none has as yet been isolated. It is generally found in children between the ages of four and fourteen; it may be epidemic, and is apt to accompany or follow improper feeding, infectious diseases, also poisoning by mercury, arsenic, lead, or phosphorus. Unhygienic surroundings and any local irritations are potent factors in this as in the other forms of stomatitis.

Symptoms.—The gums, of the lower jaw chiefly, are spongy, painful, swollen, and bleed readily; later on, the cheeks and lips become affected. The gums also recede from the teeth, which become loosened and may fall out; ulcers may also occur round the sockets of the teeth, and a purulent fluid forms between the gums and the teeth, as well as between the teeth. There are profuse salivation, very fetid breath, and swelling of the neighboring lymph glands. In chronic cases the periosteum of the lower jaw becomes involved, and areas of necrosis ensue. There is great debility, and nausea and diarrhœa, caused by swallowing the profuse fetid saliva, are also apt to be present.

Treatment is on the same lines as in other forms of stomatitis. On account of the disagreeable odor of the breath the patient should be isolated. Mouth washes are required, but in case potassium chlorate is used care must be taken that no untoward results occur, particularly in children. Hydrogen peroxide or dioxide makes an admirable mouth wash.

5. Bednar's Aphthæ, also called *Plaques pterygoidiennes*, or *aphthæ of the palate*, is a variety of ulcerative stomatitis. It is sometimes of traumatic origin, being due to pressure. It occurs generally in bottle-fed children who have unhygienic surroundings and are badly cared for, and is caused by the pressure on the hard palate of an artificial nipple or of the nurse's finger, or of a swab used in cleaning the child's mouth. But in breast-fed children it may also be found; it is then caused by the pressure of the infant's tongue on the thin mucous membrane, during the act of nursing. As a rule the affection is of a mild character, and is found on the hard palate near the alveolar process, but in badly neglected cases the ulceration may be both deep and extensive. In mild cases no special treatment is required beyond the removal of the cause; while in more severe cases a five-per-cent. solution of silver nitrate should be applied.

6. Aphthous Stomatitis.—(*Synonyms:* Follicular stomatitis, Vesicular stomatitis, Herpetic stomatitis, Aphthæ, Canker.)

In this form of stomatitis, which is more common than the catarrhal variety, the mucous membrane of the mouth is hyperæmic and is characterized by grayish or yellowish vesicles which are liable to ulcerate, and are chiefly found on the margin and frænum of the tongue, and on the cheeks; also on the inner surface of the lower lips, near the junction with the gums.

Etiology.—It is probably due to some specific germ, but none has yet been isolated. It is found most commonly in children, and, if not idiopathic, is due to improper food, indigestion, one of the fevers, lack of hygiene and general uncleanliness of the mouth.

Symptoms.—The child is fretful on account of the pain; dull and feverish; the mouth is hot; the saliva flows freely and may irritate or excoriate the chin and neck. The ulcers described above are surrounded by red areolæ and bleed readily if any attempt is made to remove the grayish-white base. The process lasts about a week.

Prognosis is good. The sores may be treated with silver nitrate; local washes of potassium chlorate or potassium permanganate should be used; food, tonics, and stimulants are required.

7. Parasitic Stomatitis.—(*Synonyms:* Mycotic stomatitis, Stomatomycosis, Thrush, Muguet, Soor.)

Thrush is one form of parasitic stomatitis, but it is the most important variety. The disease is due to a vegetable parasite, and consists of white flake-like patches on the mucous membrane of the mouth and tongue. These patches consist of epithelium, leucocytes, and the spores and filaments of a fungus. The fungus or mould has been described as oïdium albicans, saccharomyces albicans, oïdium lactis, mycoderma vini, and monilia candida. The fungus displays remarkable polymorphism, having a great tendency to spore formation in a solid medium, and to filament formation in a liquid medium. The fungus tends to grow rapidly, particularly upon an unclean surface. The spores lodge between the epithelial cells; then separating the different layers and destroying the superficial layer they penetrate down into the connective tissue. The disorder is apt to become epidemic in institutions where there are many children, being transmitted by unclean feeding apparatus. The spots or patches look like curdled milk, but are covered with epithelium and are readily removed without bleeding, being thus differentiated from aphthous or follicular stomatitis.

Etiology.—The disorder is found generally in childhood, and occurs in the debilitated or uncleanly, more particularly in bottle-fed infants. It is apt to follow catarrhal stomatitis; and the growth of the fungus is favored by mouth breathing and by the restricted movements of the tongue which are necessitated by many forms of stomatitis.

Symptoms.—The symptoms are as a rule slight and much like those of catarrhal stomatitis. The saliva is acid and decreased in quantity; and the mouth is apt to be dry.

Treatment, as in other forms of stomatitis, consists in absolute cleanliness, the employment of mouth washes of an antiseptic character, the observance of a proper hygiene, and the administration of good food, tonics, and stimulants.

8. Gangrenous Stomatitis. — (*Synonyms:* Noma, Cancrum oris, Water cancer.)

This is an uncommon but very formidable complaint, and is almost invariably found in young children. It is favored by poor hygienic conditions, lack of food, and general enfeebling diseases. It may follow an ordinary ulcerative stomatitis, but the two conditions are very

different. Probably some micro-organism is the cause of the disease, but so far it has not been isolated. Cancrum oris must not be interpreted as an ordinary gangrene of a local character, for the blood supply of the face is far too good to allow of such a supposition. Characteristics of this disease are: (1) that it begins on the inside of the cheek; (2) that it is almost always unilateral, though cases have been reported in which both cheeks were attacked; (3) that it perforates the whole thickness of the cheek; and (4) that it is rapidly fatal. At first there will be observed a small red swelling on the inside of the cheek, often opposite the opening of Stenson's duct. This small swelling gives place to a large, rapidly growing ulceration and is followed by gangrene. The destructive process begins from within and works outward. The whole thickness of the cheek is soon involved; it becomes brawny, and the outside is red and glazed; perforation soon occurs. The breath is fetid, the teeth fall out, the jaw becomes necrosed, and the whole process is marked by the extraordinary rapidity with which it advances, a rapidity so great that in from one to two weeks the patient dies either from exhaustion or from pyæmia. "The intelligence remains generally undisturbed, and the little patients do not seem to be greatly alarmed, but rather apathetic. The temperature and respiration become influenced principally because of, and in proportion to, the inflammation of the lungs, which is frequently a precedent and concomitant condition. This associated pulmonary inflammation is, however, never of the sthenic type of simple acute lobar pneumonia." (From former edition of REFERENCE HANDBOOK.) "Diagnosis in the later stage is rendered unmistakable by the ulcer, nodule, slough, and perforation. The early stage is to be distinguished from malignant pustule (anthrax). The latter begins as a pustule upon the outside of the cheek, often at the site of an abrasion; it is far more common in adults, and the anthrax bacillus is discoverable in the pustule and blood." (Thompson's "Practical Medicine.") There is very little pain, but much prostration, and generally there are nausea and diarrhœa.

The *prognosis* is bad; different writers place the death rate at between eighty and ninety-five per cent.

Treatment to be of any use must be vigorous and early. Free extirpation or the application of the cautery should be early resorted to; there should be frequent applications of hydrogen dioxide, and tonics and nourishing food should be administered every two or three hours.

9. MERCURIAL STOMATITIS.—(*Synonym:* Mercurial ptyalism.)

This is an inflammation of the mucous membrane of the mouth and gums, due to the use of mercury; it is rarely found in syphilitics.

Symptoms.—The patient complains of a metallic taste, tenderness of the gums which are also unusually red, and increased flow of saliva; the tongue becomes swollen and there is difficulty in both mastication and deglutition. The salivation is apt to be extreme; and the odor of the breath is most offensive.

Treatment.—Those working in mercury should cleanse both mouth and teeth frequently; and those taking the drug should at once discontinue its use. The best remedies are salines, alkaline drinks, and atropine to arrest the flow of saliva. During convalescence tonics will be required.

10. PTYALISM, or SALIVATION, and XEROSTOMIA have been described in Vol. VII. of the REFERENCE HANDBOOK, under the heading *Salivary Glands, Diseases of;* it only remains here to outline the treatment of the former condition. When ptyalism is produced by the administration of mercury, as is (or was) generally the case, the use of that drug should be discontinued, the mouth should be washed with astringent lotions such as alum or potassium chlorate, and potassium iodide should be given internally. Mercurial salivation can often be prevented or diminished by devoting proper care and attention to the condition of the patient's mouth and teeth; it has been asserted that the administration of small doses of potassium chlorate in conjunction with the mercury will also lessen the likelihood of salivation. In ptyalism from other causes the tincture of belladonna has been recommended in doses of ♏ x. t.i.d.

11. ANGINA LUDOVICI, or Ludwig's angina, is the name given to an infective inflammation of the floor of the mouth, and of the cellular tissue beneath the deep cervical fascia. It generally begins in the submaxillary glands, and is due to an infection with one or more varieties of the pus-producing bacteria—probably the streptococcus pyogenes—and is accompanied by much swelling and infiltration of the mouth, tongue, throat, and neck. There are severe pain and dyspnœa, the latter being often caused by œdema of the glottis. The patient finds great difficulty in opening his mouth, in talking, and in masticating and swallowing his food. Sloughing of the soft parts is apt to ensue and is called *cynanche gangrenosa*.

Prognosis is not good.

Treatment consists in the employment of antiseptic measures and in making a prompt and free incision into the involved tissue, generally in the median line. Tracheotomy may be demanded for œdema of the glottis. Tonics and nourishing food are indicated. (See also Vol. VI., p. 593.)

12. PERLÈCHE is a contagious disorder consisting of fissures at the angles of the mouth. The trouble is found chiefly in children, and is very painful. It is probably caused by a micro-organism; Le Maistre reporting a streptococcus, and Raymond a variety of staphylococcus in connection with this disorder. It lasts for from ten to twenty days, and is bilateral, beginning at the angles of the mouth, and spreading along the border of the lips. The lips swell and are painful, and are apt to ulcerate. The skin around the mouth is not often attacked, but the mucous membrane is involved and the epithelium becomes white and sodden and is then desquamated. Pain and itching are present, and the child licks the parts to relieve the pain and burning; hence the name, from the French perlécher (= to lick). The disease is spread by drinking-vessels. Treatment consists in cleanliness and the use of astringent lotions of alum, copper sulphate, or even nitrate of silver. A dusting powder of bismuth subnitrate may be used; and, as a prophylactic measure, children should have their own cups to drink out of.

13. RIGA'S DISEASE occurs as a gray ulcer with an irregular border situated under the tongue, near the frænum. It appears about the period of first dentition, and lasts for a variable period, usually about a year. It has been found almost epidemic, certainly endemic, in Southern Italy. Its origin is most likely traumatic. The treatment is that of catarrhal stomatitis.

14. SALIVARY CALCULUS may occur in the excretory duct of any of the salivary glands, but is most frequently found in Wharton's duct. It consists of phosphate and carbonate of calcium together with sodium chloride and magnesium. After such a concretion is formed, it may either remain in the gland, or be discharged through the duct, or it may obstruct the duct. In the two former conditions it gives no trouble, but in the last case it gives rise to pain and swelling of the gland with which it is connected; the swelling is always increased on taking food. Careful palpation along the course of the duct will help in making a diagnosis; and, except in mumps, pain and swelling in a salivary gland should always suggest salivary calculus.

Treatment consists in making an incision into the duct, either in the distended portion only, or in its whole length from the outlet to the obstruction. If left untreated the duct may burst, with formation of a salivary fistula.

15. SALIVARY FISTULA is an abnormal opening of the duct of a salivary gland, and may be either internal or external, according as it opens on the inside of the mouth or on the outer surface of the cheek. Such a fistula is due to wounds of the duct, or to a rupture of the duct from suppuration or calculi. The parotid gland is the one most commonly affected. Internal salivary fistula is of comparatively little consequence, as the saliva flows into

the mouth. But in external fistula the flow of saliva on the cheek causes considerable discomfort

Treatment.—If a calculus is present it must be removed. Then find the internal opening of the duct, and see if it is patent; if it is not patent, an artificial internal fistula must be made; and the edges of the external fistula can be touched with a cautery or pared, and closed with a twisted suture.

16. Tongue-tie is practically a congenital shortening of the frænum linguæ. The tongue cannot be protruded beyond the teeth; and suction and, later, articulation are interfered with. The proper treatment is division of the frænum, generally on the notched shield which forms the handle of a grooved director. Care must be taken to avoid wounding the ranine arteries. Blunt-pointed scissors should be used, and the points directed toward the floor of the mouth and away from the under surface of the tongue. Often the frænum is simply nicked with the scissors and the operation completed with the finger nail.

17. Pyorrhœa Alveolaris, or Rigg's disease. In this condition there is found a shrinkage of the gums and alveolar border, together with separation of the gums from the teeth, which become loosened and may fall out. It is due to an inflammatory condition of the gums combined with bacterial infection and an excess of tartar. General cleanliness is indicated, with removal of the tartar; antiseptic and astringent mouth washes and general tonics should also be prescribed. Treatment may have to be continued for a long time as the condition is often intractable; and the patient may expect to lose some of his teeth.

18. Alveolar Abscess is the result of inflammation and suppuration in connection with the fang of a carious tooth. It may occur in either jaw. Pus forms in the socket of the tooth and either finds its way out by the side of the tooth or through the gums, in which latter case it is called a gumboil or parulis; occasionally it strips the periosteum from the bone and forms an abscess of large size, and may even produce necrosis of the jaw. The first indications of the trouble are pain and a feeling as if the tooth were a little longer than normal. If the abscess is allowed to remain, there may be severe constitutional symptoms. Incision is indicated, and if it be delayed the tooth becomes loosened and exfoliation of the periosteum with necrosis may occur. In the upper jaw pus from a neglected alveolar abscess may burrow into the antrum of Highmore and set up suppuration there, or it may discharge by way of the nose. In the lower jaw the pus may travel downward and point and burst in the neck.

Treatment consists in disinfection of the mouth, incision of the gum, and extraction of the tooth. As a prophylactic, children should be taught to use a tooth-brush, and their teeth should be regularly attended to by a competent dentist.

19. Epulis.—This term is applied to a tumor growing from the fibrous tissue of the gum or from the alveolar periosteum. The name is derived from *ἐπὶ* and *τὸ οὖλον*, and means literally a tumor situated "on the gum." There are two varieties: the simple or fibromatous, and the malignant or myeloid. They generally attack the lower jaw.

Simple or fibromatous epulis appears as a rounded, smooth mass, sometimes lobulated or sessile; it is firm or elastic to the touch, and of a color varying from pinkish to deep red. It is generally due to carious teeth and is more apt to be formed on the outer border of the gums, though it may appear between two teeth, causing more or less displacement, and also on the inner surface of the gum. It is covered with epithelium, and may contain a few spicules of bone derived from the maxilla. The presence of the latter is much more common in the malignant or myeloid variety.

Treatment consists in the free removal of the tumor together with any teeth, stumps, or bone that may appear to have some causal relation to the growth. It is well, therefore, to extract a tooth on each side of the epulis, to cut through the whole thickness of each alveolus vertically with a small saw, and then finally to join these incisions at their lower ends by a horizontal incision made with a chisel. Thus the continuity of the jaw will remain notwithstanding the fact that a quadrangular piece of bone has been removed.

Malignant or Myeloid Epulis.—This is really a myeloid sarcoma and springs from the alveolar process. The chief distinction between these two varieties is pathological; the clinical picture being much the same as in the simple variety, except that the mucous membrane covering the tumor is more apt to ulcerate, and there is always a connection with the underlying bone. The treatment, too, is the same, only the malignant variety sometimes requires very energetic and radical treatment.

20. Wounds and Injuries of the Mouth have, for the most part, the same features as are presented in wounds and injuries elsewhere. The blood supply of the mouth being particularly abundant, there is apt to be profuse hemorrhage, but this same abundant blood supply causes the processes of repair and healing to be very rapid. Hemorrhage from the mouth is due to wounds, injuries, purpura, biting the tongue, plethora, scurvy, and the hemorrhagic diathesis; it is best controlled by the application of cold or pressure. In slight cuts of the lips a little cotton soaked in collodium makes a good protective and also stops the bleeding. In wounds of the mouth we must remember that the buccal cavity always contains bacteria capable of producing infection, and therefore asepsis is not attainable; but antiseptic mouth washes should be used as frequently as possible.

21. Burns and Scalds of the Mouth.—These are generally caused by accident, and are due to hot liquids introduced into the mouth, to chemicals (acids and alkalies), or to inhalation of hot air or steam. They are most commonly met with in children, owing to their greater liability to drink out of the spout of a kettle or teapot. Adults are more likely to suffer in explosions, under which circumstances they may inhale steam or ignited gas. The inside of the mouth and pharynx are involved, and œdema of the glottis is a probable complication. The symptoms are intense burning pain, dyspnœa, suffocating cough; the lips and mucous membrane of the mouth are either white, sodden, puffy, and blistered, or the mouth may escape and show little or nothing of the hurt. In this latter event the glottis may be scalded, when the edges of the epiglottis will be scorched and the larynx also involved.

Treatment is the same as that for burns in other parts of the body: (1) *constitutional*, to combat shock and to keep up the patient's strength; and (2) *local*, in the form of mild antiseptic mouth washes and cool mucilaginous drinks. For œdema of the glottis tracheotomy may be required. There may be cicatricial contractions resulting in great deformity, and, for the relief of this deformity, extensive plastic operations are often performed.

22. Errors of Development.—The chief of these are harelip and cleft palate, both of which are considered in other parts of the Reference Handbook. Among the other defects, of which mention may be made here, are the following:

Astomia, or absence of the mouth; this, of course, is incompatible with life.

Atresia oris differs from the above in that there is a buccal cavity, but no external opening. This defect is generally combined with other errors of development. The line of the closure is more or less apparent, and the membrane may be thin or tough and dense. As in similar conditions elsewhere incision is required, but care must be taken lest the freshened edges grow together again.

Microstomia, or congenitally small mouth, is a milder form of atresia oris, and is due to the fact that the parts that form the lips have fused to a greater extent than normal, thus causing stenosis of the buccal orifice. The mouth may be so small that the infant cannot nurse. In such a case it must be enlarged sufficiently and the mucous and cutaneous borders stitched together.

Macrostomia, or congenitally large mouth, is gene-

rally unilateral, and is said to occur more frequently in females. It is found in connection with other developmental errors, and is usually due to the non-union of the mandibular and maxillary processes, or to the persistence of the lachrymal fissure. The treatment consists in paring and uniting the edges of the cleft sufficiently to reduce the mouth to normal dimensions.

R. J. E. Scott.

In preparing this article use has been made of the following: The former edition of the REFERENCE HANDBOOK; Ziemssen's "Cyclopædia"; Reynolds' "System of Medicine"; Pepper's "System of Medicine"; Allbutt's "System of Medicine"; Keating's "Cyclopædia of the Diseases of Children"; Thompson's "Practical Medicine."

MULTIPLE (CEREBRO-SPINAL) SCLEROSIS.—(Synonyms: Disseminated sclerosis; Insular sclerosis.)

DEFINITION.—This disease may present manifold symptoms, the most common of which are paresis, with muscular rigidity and exaggerated tendon reflexes as in spastic paralysis, tremor brought on by voluntary movements, nystagmus, scanning speech, amblyopia, apoplectiform attacks, and impaired intellect. The anatomical basis of the disease consists of disseminated patches of sclerosed tissue in various parts of the central and peripheral nervous systems.

ETIOLOGY.—An hereditary influence has been traced in a few instances. Charcot states that the disease occurs most frequently in females, but a number of other observers do not concur with him in this view. It occurs most frequently between the ages of fifteen and thirty; occasionally in young children; rarely, if at all, after forty.

Traumatic influences, such as blows on the head, concussion of the whole body, exposure, hardship, overwork, and profound emotional disturbance, may all be mentioned as occasional exciting causes. In a number of instances the disease developed after the existence of an acute disease, typhoid fever, variola, etc.

SYMPTOMS.—The area of diseased tissue may be located in any part of the nervous system and there may be quite a number of affected areas. Furthermore, the disease may be of various degrees of severity, and the symptoms, which are but the expression of the locality and intensity of the disease, may make the most varied clinical pictures. There may be an entire absence of symptoms of disease of the nervous system, although nodules of sclerosed nerve tissue are found post mortem; or the disease may simulate various different organic or functional nervous diseases. But, nevertheless, the sclerosis seems to have a predilection for certain parts of the nervous system, and we find, accordingly, in many cases similar, and almost characteristic, clinical manifestations.

A cerebral and a spinal form of multiple sclerosis are sometimes spoken of, but usually both brain and cord become involved in the disease, though it may have been present in the one some time before it developed in the other. Generally the spinal cord is first affected.

The disease usually begins very insidiously and is slow in its progress; in rare instances it has an abrupt beginning, perhaps is ushered in by an apoplectiform attack. The earliest symptoms may be of cerebral origin, such as headache, vertigo, ataxic gait, and slight psychic disturbances; or there may be a slight tremor in one or both hands; but more frequently the symptoms are those of spastic paralysis.

At first there is weakness of one leg, then of both, attended by some difficulty in walking. Gradually, with increasing paresis of the limbs, there appear muscular rigidity, especially brought on by active or passive movements, exaggerated tendon reflexes, spastic gait, and, finally, rigid contractures of the limbs. The paresis, and, to a less extent, the muscular rigidity, etc., at a later period affect the upper extremities, and to these is subsequently added another motor symptom—one of the most prominent and characteristic of this disease—the so-called intention tremor, *i.e.*, tremor during the performance of a voluntary act. Before it is otherwise noticeable, it may be observed in the handwriting or other delicate movements of the fingers, especially if the act is slowly performed. The writing, if carefully observed, will be seen to be full of small indentations which occur with great regularity, indicating that the tremor is rhythmical. When the tremor is well marked any voluntary movement will cause it to appear, and it may be seen to some extent during rest. A common method of eliciting the symptom is to ask the patient to put a glass of water to his lips. The tremor increases and the oscillations of the hand are greater as the latter approaches the mouth. The trembling may become so violent that all the water is thrown out of the glass. When the patient is sitting quietly either there is no tremor, or slight movements of the head and trunk may be observed. If he now perform a voluntary act, as lifting an arm, the tremor in the head and trunk increases at the same time that there is tremor of the acting member. When he attempts to walk there may be such violent tremor of the limbs and trunk as to make walking, or even standing, almost impossible. On the other hand, when the patient lies down and every part is well supported no tremor appears. None is observed during sleep. It is increased by emotional excitement.

All the voluntary muscles may be thus affected, the head as well as the trunk and limbs. Tremor in the face is less commonly seen, though there may be irregular movements, choreic in character.

The distinctive features of the tremor are that it is rhythmical, and that it occurs only with muscular efforts. A very few cases have been reported in which it continued even in rest, but such cases are exceedingly rare. The tremor is not found in all cases. It probably depends on the locality of the disease. It also disappears in any part when the latter has become completely paralyzed.

The tremor can usually be easily distinguished from that of other diseases. In paralysis agitans, in the beginning (and it is only then that the two diseases could easily be confounded), only a few fingers are affected, and the oscillations are fine and very rapid. At the same time the tremor has somewhat the character of coordinated movements. Thus the movement of the thumb upon the fingers has been likened to that of counting money, rolling pills, etc. The tremor of multiple sclerosis is large and coarse, with no appearance of coordinated action. In paralysis agitans, furthermore, the tremor is, to some extent, controlled by voluntary movement, and increases with rest, and the head is very rarely affected. When the tremor is violent it may have the appearance of the movements of chorea. But the latter occur during repose as well as during volitional acts, and they cause an intended movement to be made very irregularly; on the other hand, in multiple sclerosis the general direction of any movement is maintained, but the line of movement is an undulating one, the undulations playing equally up and down along the central line of direction.

The next two symptoms seem to be similar in character to the tremor. The first is nystagmus, a very common symptom, and of value in diagnosis. When not otherwise noticeable, it may be made manifest by movements of the eyes, strong convergence, or forced movements in some direction. The other symptom is scanning speech. Other changes of speech are sometimes present, but this is the most common and most characteristic, and, therefore, of high diagnostic value. The speech is slow and dragging, each syllable being pronounced separately as in the slow scanning of verse, and, therefore, termed scanning speech. If the patient attempts to speak more rapidly, his words are likely to be so jumbled together as not to be at all understood. The voice is monotonous to the highest degree. There is often tremor of the lips at the same time, and, on laryngoscopic examination, there has been found to be diminished tension of the vocal cords.

Other ocular symptoms besides nystagmus are frequently found. Double vision, due to paralysis of some

of the external muscles of the eye, occurs, just as in locomotor ataxia, either as a transient symptom at an early period of the disease, or as a permanent condition at a later stage. Amblyopia is also a common symptom. Generally there is only impaired vision, not complete blindness. The ophthalmoscope reveals, in these cases, a discoloration of the discs, due to a degree of atrophy of the optic nerves.

Headache and vertigo are often present, both in the early and in the later stages of the disease. The vertigo often occurs in paroxysms. Occasionally it is due to the double vision, but more frequently it is quite independent of the latter condition.

The mental symptoms often play an important rôle. Sight psychic symptoms may be manifested in the beginning of the disease if the latter first affects the brain, but the graver symptoms are, usually, late manifestations. Change in disposition, irritability, loss of self-control, a tendency to laughing and crying, are common conditions. A certain impairment of intellect—weakened memory, a degree of apathy, etc.—is also not uncommon. But a high degree of dementia is rare. It is likely to occur only when the disease begins at an early age and there is arrested development of the brain, or when the pathological process is very acute. Different forms of insanity are sometimes observed, most frequently melancholia, occasionally delusional insanity.

Apoplectiform seizures, like those seen in general paralysis, are important symptoms. They occur, according to Charcot, in one-fifth of all cases. After slight prodromal symptoms, headaches, etc., coma develops within a few hours, the temperature rapidly rises, often reaching 104° or 105° F., and at the same time the face is flushed and the pulse rapid. Hemiplegia, with flaccidity of the paralyzed muscles, is soon observed. Within a day or two consciousness returns, the temperature falls, and, within a comparatively brief period, the paralysis disappears. Such attacks may occur every few months, or very rarely. They usually leave the patient in a permanently worse condition, thus marking the progress of the disease. Sometimes the patient dies in the attack. These seizures are very much like those of apoplexy, but post-mortem examinations reveal no anatomical basis for them.

In the foregoing have been given the most common symptoms of multiple sclerosis, those found in the majority of cases. But, on account of the distribution of the diseased areas, various other symptoms may be manifested. Thus the disease may attack the posterior columns of the cord, and ataxia, pain, anæsthesia, paræsthesia, etc., will be present; or it may involve the gray matter, when atrophy and paralysis of muscles will ensue. Or the disease may involve the whole thickness of the cord and produce the symptoms of transverse myelitis. When the posterior as well as the antero-lateral columns are affected, many of the appearances of spastic paralysis are likely to be absent, especially the exaggerated tendon reflexes. Symptoms referable to the bladder and to the rectal and genital functions are also likely to appear. If the disease involve the nuclei of the facial, hypoglossal, and pneumogastric nerves, the ordinary symptoms of labio-glosso-laryngeal paralysis will be manifested, and various local cerebral symptoms may appear, according to the location of the foci of disease.

The course of the disease is a very chronic one. Charcot has divided it into three stages—a division applicable to those cases which present the common clinical picture.

The first stage is from the beginning of the disease to the period of complete disability from paralysis and contractures of the limbs. This stage may last for from two to six years or longer. The symptoms are very slow in their progress. They begin as spinal or cerebral, but both sets of symptoms appear before this stage is terminated. There is often an arrest of the symptoms, or even improvement, which indefinitely prolongs this stage, and may give rise to delusive hopes of complete restoration to health.

The second stage, that of the fully developed disease, may last also for from two to six years. There seems to be little change in the patient during this period, and, though entirely helpless, he seems not to suffer in general health.

The third stage is that of decline. The general health is affected, there are loss of appetite, wasting, etc. Cystitis, decubitus, pyæmia, etc., may hasten the end. Or the latter may be due to an increase in the bulbar symptoms, or to an apoplectiform attack. More frequently a fatal termination is caused by an intercurrent affection—pneumonia, typhoid fever, or, above all, phthisis.

The average length of the disease is from six to eight years. In rare cases it terminates in a year or two; occasionally it lasts twenty years.

Morbid Anatomy.—The pathological changes can usually be seen by the naked eye. They consist of numerous patches or nodules of sclerosed tissue scattered throughout the nervous system. The nodules vary in size from merely microscopical proportions to an object as large as a chestnut or larger; they are rounded or irregular in shape, and may often be seen on the surface as slight prominences or depressions, but are found in larger number when sections of the brain and cord are made. Their color is mostly of a gray or reddish-gray; they are translucent, and have a firm, often cartilaginous, consistence. Many of the nodules are of the same color as the surrounding tissue, and are only distinguished by their consistence. In rare instances a few may be softer than the normal tissue, probably indicating recent disease; most of the nodules, on the other hand, are firmer than the normal tissue, doubtless being of very old standing, for such cases come to the post-mortem table only after the disease has existed a long time. The nodules seem to be quite distinctly circumscribed, but the microscope reveals the fact that they merge imperceptibly into the healthy tissue. They are also quite distinct, as a rule, though occasionally they blend into one another. In rare instances there has been found, in both the brain and the spinal cord, a diffuse sclerosis which, to some extent, has united the scattered nodules. On the other hand, secondary degeneration seems rarely, if at all, to develop from the disseminated disease.

The number of nodules found in a single instance may be very small, or may run into hundreds. Their distribution in the cord is very irregular. In some sections they may be found in the anterior, in others in the posterior, columns; in still others in the gray matter, or they may involve all these parts in the same section. Usually a large number of nodules are found in the medulla, pons, and crura cerebri. It is very rare that these parts are found free from disease. In the hemispheres the walls of the ventricles, corpus callosum, and centrum ovale are favored seats of the disease. In the latter two localities the nodules are often quite large. Usually nodules are also found in the large ganglia, while the cortex generally escapes. But few nodules are, as a rule, found in the cerebellum, and these in the central white matter. Similar nodules may be found in the nerves, most frequently in the optic nerves, but occasionally in the hypoglossal, the nerves of the eye, and the roots of the spinal nerves.

The microscopical appearances are those of interstitial myelitis. The nodules are mostly new connective tissue composed of very fine wavy fibrillæ. But in this new tissue the axis cylinders of the nerve fibres can usually be found in large numbers, though their medullary sheaths have disappeared. This is especially true of the nodules in the spinal cord.

At one of the meetings of the Society of German Naturalists and Physicians, Adamkiewicz expressed the opinion that the disease is not interstitial, but develops primarily in the nervous tissue, beginning in the medullary sheaths of the nerves. He bases his opinion upon results obtained by a new method of staining the nervous tissue. His view is altogether at variance with that formerly held, and may be looked upon with doubt, at least until further corroboration is forthcoming.

Morbid Physiology.—Many of the symptoms are

easily explained by the lesions found: psychic symptoms by disease of the hemispheres, bulbar symptoms by lesions of the medulla, muscular atrophy by lesions in the anterior cornua, anæsthesia and ataxia by disease of the posterior columns, spastic paralysis by disease of the antero-lateral columns—in some instances cerebral lesions may produce the same symptoms,—while amblyopia and some other symptoms are often due to nodules in the nerves themselves.

The long retention of the axis cylinders accounts for the usual presence of paresis rather than paralysis, for the anæsthesia being slight, for the amblyopia rarely advancing to complete blindness, etc. (In locomotor ataxia there are also numerous axis cylinders in the sclerosed area, and the symptoms usually point to only a partial loss of function.) Charcot attributes the tremor to the same condition. He supposes that the axis cylinders continue to carry voluntary impulses, but, because they are bared of their medullary sheaths, they carry them in an irregular, jerking manner, and hence the oscillations in the voluntary movements. While this must be considered a mere theory, we can speak with more positiveness of the location of the lesion as a cause of the tremor. It seems to be due to nodules in the medulla and pons, or, at least, in the basilar portions of the brain. In a few cases, in which the disease was limited to the cord, no tremor was observed. On the other hand, when tremor was observed during life nodules were always found in the medulla and pons; when it was not observed, these parts were not affected to any extent.

With a considerable degree of doubt, we may attribute the nystagmus to lesions in the corpora quadrigemina, the scanning speech to lesions in the medulla, the vertigo to lesions in the medulla or cerebellum. A satisfactory explanation of the apoplectiform attacks has not yet been given.

Diagnosis.—In some instances a diagnosis is made with the greatest ease, in others it is almost impossible to make a diagnosis. The most common clinical picture—paresis of the extremities with exaggerated tendon reflexes, intention tremor, nystagmus, scanning speech, amblyopia, etc.—is so characteristic that it cannot be mistaken.* But some of the most characteristic symptoms may be wanting, and then the diagnosis is much more difficult. In this case the indications of multiplicity of lesions and the very chronic course of the malady must be the guides to diagnosis. When the disease is limited to the spinal cord one can scarcely do more than guess in distinguishing it from other forms of myelitis. In such cases one must be on the lookout for cerebral symptoms. Optic atrophy is often a valuable diagnostic symptom, not only in this instance, but in excluding hysteria or other functional diseases which may simulate multiple sclerosis.

When the sclerosis affects only the brain it may present some of the manifestations of brain tumor. Here, too, the indications of a multiple lesion and the very slow course of the disease may clear up the diagnosis. But there is another important distinction, in that brain tumors produce to a large extent general symptoms, those of intracranial pressure, such as severe headache, convulsions, and double optic neuritis; while sclerosis produces merely local symptoms, those indicating the loss of function of the part affected by the disease.

The tremor of alcohol, lead, and mercurial poisoning might be mistaken for this disease, but concomitant symptoms and the history of a cause will establish the diagnosis. The tremor of paralysis agitans, with which this disease was formerly confounded, is easily distinguished by the appearance of the tremor, its being controlled to some extent by voluntary effort and increased during rest, and its very rarely affecting the muscles of the head and neck. Furthermore, paralysis agitans is rarely found in persons under forty years of age, while multiple sclerosis rarely occurs after thirty, and, apart from the tremor, the symptoms of the two diseases are quite different.

Prognosis.—Charcot believes that the disease may sometimes be cured, but the opposite view is generally entertained, though its arrest and even improvement for a number of years have been observed. It usually runs a very protracted course. When at its inception it manifests itself in various parts of the nervous system at the same time, it is likely to run a more rapid course. The occurrence of apoplectiform seizures, cystitis, bulbar symptoms, etc., indicates the approach of a fatal termination.

Treatment.—The same treatment is applicable as in other forms of chronic myelitis. (See *Spinal-Cord Diseases* in Vol. VII.)

Philip Zenner.

* Schuler reported a case of tumor of the right hemisphere, in the neighborhood of the island of Reil, which produced the typical clinical picture of multiple sclerosis, and Westphal reported two cases with similar histories, in which no pathological changes were found post mortem. But these are such rare occurrences as not materially to impair the diagnostic value of this clinical picture.

NERVI.—The town of Nervi stands upon a narrow, shelf-like plateau which intervenes between the base of an outlying spur or side range of the Apennines and the shore of the Mediterranean Sea, at a point some six miles distant from Genoa, in a southeasterly direction. The general trend of the coast line along what is known as the Riviera di Levante, or Eastern Riviera, between Genoa and Spezia, is from northwest to southeast; but, as in the case of the Western Riviera, the regularity of the line is frequently interrupted by the occurrence of bays, which are guarded by rocky headlands, jutting into the sea from the main chain of the Apennines, just as similar headlands along the Western Riviera reach down to the sea from the Maritime Alps. The scenery along this coast is consequently very similar to that of the Western Riviera, and, as the writer can testify from personal experience, it is exceedingly picturesque and beautiful. The width of the little plateau upon which Nervi is built does not exceed a quarter of a mile; its elevation above sea-level is very inconsiderable, and probably does not exceed one hundred feet. The shore line at Nervi runs nearly due east and west; the spur or side chain of the Apennines already mentioned, consisting of three separate mountain peaks, extends parallel with the shore, immediately back of the town. The most westerly and terminal peak of this side range is only about seven hundred or eight hundred feet high, and it is covered to its top with a growth of olive trees; the other two peaks are much higher (about twenty-five hundred feet), and their summits consist of bare rock.

The town of Nervi has a population of a little over three thousand, and it is built, in the straggling fashion so familiar to travellers who have visited the Italian coasts, along the old Genoa and Spezia post road. At this point the road does not skirt the shore, but hugs the base of the hills, so that the town stands close under the shelter of their steep slope, and is effectually protected from northerly winds. From easterly winds it is, in common with all points along the Eastern Riviera, protected in great measure by the main chain of the Apennines. The northeast wind is not effectually kept out, but gains access through gaps in the hills, and is sometimes strongly felt at Nervi. "The northwest wind," says Dr. Sparks, "is also not unknown, and Dr. Thilenius says of it, 'The most dangerous wind and the wind which is always the most violent, is the cold, cutting, dry, and bitter northwest.'" The warm, damp, relaxing "scirocco" wind, blowing from the southeast, is also of frequent occurrence.

The rainfall at Nervi is heavier than along the Western Riviera. The average fall in each of the six colder months of the year, derived from seven years of observation, is quoted by Dr. Sparks from Dr. Thilenius as follows: November, 6 inches; December, 4.88 inches; January, 4.78 inches; February, 3.23 inches; March, 4.49 inches; April, 2.20 inches. In the winter of 1876–77 the number of rainy days, including days on which slight showers occurred, during the months of December, January, February, and March, was 48. At Mentone, during the same period, 27 such days occurred (Sparks). This

season is spoken of by Dr. Sparks as a comparatively dry one. The winter of 1874–75, on the other hand, appears to have been at Nervi an exceptionally wet one, for Dr. Sparks quotes Dr. Thilenius to the effect that during that season "it rained almost incessantly for three months, day and night, and the air was so saturated with moisture that there was scarcely any difference between the wet- and dry-bulb thermometers." In the comparatively dry seasons of 1875–76 and 1876–77 the mean relative humidity, measured by August's psychrometer, and quoted by Dr. Sparks from Dr. H. J. Thomas, of Baden-Weiler, was as follows:

	Dec.	Jan.	Feb.	March.	April.
1875-76	64.0	60.0	64.8	66.7	72.7
1876-77	75.0	63.2	61.4	68.5	....

Dr. Kisch[3] gives the mean relative humidity of Nervi as 62.9 to 66.6 per cent. So far as these figures go, they appear to indicate greater dryness of the atmosphere at Nervi than exists at Mentone, yet Drs. Weber[2] and Sparks[1] both pronounce the climate of Nervi to be moister than that of Mentone.

At Genoa, which, it will be remembered, is only six miles distant, the mean relative humidity is decidedly less than it is at Mentone, and during the prevalence of northerly winds it falls very low indeed, below twenty per cent.; occasionally as low as eight or nine per cent. On the other hand, when the "scirocco" blows, the air at Genoa becomes very moist. Dr. Hann, in his "Handbuch der Klimatologie," gives the mean relative humidity of Genoa, for the five months November to March, as fifty-seven per cent. Now the free exposure of Nervi to the moisture-laden southerly winds and its shelter against the cold, drying, northerly winds characteristic of the Genoa climate, would no doubt combine to effect a great modification of the mean of humidity at the former place when compared with that of the latter; a modification, namely, in the direction of a higher percentage of saturation. Yet, taking into account the close proximity of Nervi to Genoa, and the relative humidity *figures* for Nervi given in Dr. Sparks' book, it seems not impossible that this writer and Dr. Weber, in pronouncing the Nervi winter climate moister than that of Mentone, have confounded the two factors of rainfall and humidity. The rainfall of Genoa is far greater than it is along the Western Riviera; the mean relative humidity is, on the other hand, very considerably less; and no better example than this feature of the Genoa climate can be adduced in support of what has already been said in the article on *Climate* (first edition), viz., that "The humidity of the atmosphere can by no means be measured by the amount of the rainfall." Probably the variations in the atmospheric humidity at Nervi are much greater in amount and more frequent in occurrence than they are at Mentone. "In spite of its raininess," says Dr. Sparks, "the soil of Nervi —clay slate—is favorable to its rapid drying."

As to the winter temperature of Nervi, it appears to be about the same as that of Mentone. Dr. Kisch[3] tells us that the temperature of the two places is similar in respect to its mean and to its variations. The observations of General Brocchi, during the years 1849–64, give the mean temperatures of November and December for thirteen years, and those of January, February, March, and April for fourteen years; they are quoted by Dr. Sparks[1] as follows: November, 55.31°; December, 47.84°; January, 46.36°; February, 47.8°; March, 49°; April, 58.1°.

The absolute reliability of these figures is not vouched for by Dr. Sparks, as he explains that he "knows nothing of the arrangement of the instruments or hours of reading."

The following table, showing a comparison of the Nervi and Mentone temperatures for a single winter, is quoted from Dr. Sparks' book, its figures being derived from calculations by Dr. Sparks, based upon observations published by Herr Schulze, in his work on the health resorts of the Riviera, and of Middle and Lower Italy.[4]

Temperatures at Nervi and at Mentone, Winter of 1874-75. (Sparks.)

	Nov.	Dec.	Jan.	Feb.	March.
Mean temperature at 8 A.M.					
Nervi	56.0	52.0	51.0	44.0	49.0
Mentone	54.0	48.2	50.5	44.5	49.8
Mean temperature at 2 P.M.					
Nervi	59.5	56.5	58.0	50.3	55.4
Mentone	59.2	53.6	56.0	59.0	57.5
Maximum temperature.					
Nervi	70.5	56.0	66.0	61.0	64.0
Mentone	70.5	64.0	64.0	55.0	66.0
Minimum temperature.					
Nervi	44.0	41.0	44.0	36.0	44.0
Mentone	46.0	42.0	46.0	36.0	48.0

The following data for mean temperature at 8 P.M. and for absolute minimum temperature at Nervi, during the months of December, 1876, and January, February, and March, 1877, are quoted by Dr. Sparks from an article by Dr. H. J. Thomas in the *Berliner klinische Wochenschrift*. The figures for the mean temperature are as follows: December, 51.5°; January, 49.3°; February, 47.2°; March, 47.4° F. The minimum temperature observed was 35.2° on March 2d, 1877. It is worthy of note, in connection with this last-quoted figure, that a minimum temperature of 25.5° was recorded in the "West Bay" of Mentone during this same month. Moreover, if one may judge from a table of monthly highest and lowest temperatures at Mentone which is given by Dr. Sparks in his account of that place, it would appear that this winter season of 1876–77 was not an unusually warm one on the Western Riviera, and that March, 1877, was exceptionally cold; and it is reasonable to infer that such was also the case along the Eastern Riviera. If such was the case, and if Dr. Thomas' observations were made under like conditions with those of Messrs. Freeman and Andrews at Mentone, the greater mildness, or, at least, the greater equability of the Nervi as compared with the Mentone climate would be illustrated, although not accurately measured, by these two figures alone.

On the other hand, Dr. Thomas' 8 P.M. figures, when compared with the daily mean figures of Dr. Brocchi, already quoted, show a decided discrepancy between the two sets of observations, especially if we assume, on the authority of the Mentone figures, that at Nervi the winter of 1876–77 was no warmer than the average.

It is to be regretted that no fuller, more extended, and more accurate observations respecting the various climatic factors of the place have as yet been made and recorded at Nervi. Nevertheless, so far as temperature is concerned, the climate is undoubtedly a mild one, and almost identical in this respect with that of the Western Riviera. As remarked by Dr. Sparks: "In spite of the want of really scientific observations on the climate of Nervi, there is no doubt of the mildness of its climate. The abundant subtropical vegetation, and the growth of standard lemon trees, is a proof of this." The following quotation from an article by Dr. Edward Haughton (London *Lancet*, December 13th, 1884) is interesting as illustrating the agency of mountain shelter in the production of Nervi's mild winter temperature. In February, 1884, this gentleman visited Genoa, Pegli, and Nervi, all on the same day, for the express purpose of making observations on this point. "The result," as he tells us, "was that the wind, which was bitterly cold at Genoa, was much milder at Pegli, especially in the valley behind the town, while it was perfectly calm, and even warm at Nervi, so long as the headlands which protect the place were not rounded by the visitor." The same point is further exemplified in a striking manner, although on a small scale, in what Dr. Sparks tells us concerning a sheltered coast-walk at Nervi itself; and everywhere along this part of the Italian coast we find that shelter from cold wind and exposure to the sun combine in varying degrees to cause marked elevation of temperature, even "in the dead of winter." At Nervi the railway runs between the town and the sea. "Below the rail-

way, and just before the rocky shore takes its deep descent into the sea, a path a few feet wide has been cut along the edge of the rock for the use of the coast guardsmen, and as it accurately follows the indentations of the coast line, and is absolutely protected from the north by high garden walls, or by part of the rocky slope, or the railway embankment, while it gets all the southern sun in its full force, it is naturally an excellent promenade for invalids. Here they can walk or sit, or, if they choose, at certain points descend close to the sea, and enjoy a temperature of 64°–68° F., while in the High Street of Nervi the thermometer at the same time is not higher than 43° or 44°. Naturally great care is necessary to be provided with plenty of wraps to put on when returning from the shore to the town."

Of amusements for the invalid there appears to be a great dearth at Nervi, and the facilities for the making of excursions in the immediate neighborhood are exceedingly limited. "The neighborhood of Nervi," says Dr. Sparks, "offers but a limited field for excursions owing to the nearness and steepness of the high hills at the back of the town. There is no drive along the shore close to Nervi, though further west the road at some places nearly overhangs the sea. . . . For amusements of all kinds, except rod-fishing, Nervi presents little opportunity."

[There are three first-class hotels at Nervi and various pensions. A train runs every quarter of an hour to and from Genoa. "The mild but tonic climate of Nervi has for some years been attracting every season an increasing number of visitors."[5] English physicians are to be found at Nervi.—*E. O. O.*]

Concerning the class of invalids who should be recommended or permitted to pass a winter at Nervi, it is impossible to decide with any degree of precision until a longer and more thorough series of meteorological observations shall have given us a more accurate knowledge of the local climatic peculiarities. For the present it can only be said that the general features of the climate are those of the Italian Riviera, and that the local modifications are such as render the climate less exciting than that of the Western Riviera resorts. *Huntington Richards.*

REFERENCES.

[1] The Riviera, by Edward J. Sparks, M.A., B.M., Oxon.
[2] Ziemssen's Handbuch der allg. Therapie und Klimatotherapie.
[3] Eulenburg's Real-Encyclopädie, art. Nervi.
[4] Die klimatischen Curorte der Riviera, Mittel- und Unter-Italiens.
[5] The Riviera, by C. B. Black, 1901.

NEURENTERIC CANALS.—It is now known that during the very early stages of the development of many vertebrates there is an open communication between the posterior portion of the medullary canal (spinal cord) and the entodermic or intestinal canal. To this communication the name of neurenteric canal has been applied. The original opening of the archenteron is known as the blastopore (see Vol. II., p. 4). In mammals, as in other amniota, it is represented by the posterior opening to the exterior of the notochordal canal. It has now been observed in various vertebrates that as the neural ridges or medullary plates develop backward they terminate against the sides of the blastopore, which acquires an elongated form. By their further growth the medullary plates close over across the long blastopore, in such a manner as to divide it into an anterior portion and a posterior portion. The posterior portion remains permanently open in certain amphibia and thus gives rise to the anus, or it may close over (Fig. 5159, *bl.*, and subsequently open, thus giving rise indirectly to the anus. The anterior portion is an opening enclosed within the medullary plate or groove, and may remain open until after the groove has closed to form a canal (Figs. 5159, 5160, *ne*), the true neurenteric canal, which establishes a direct communication between the neural and entodermal tubes. It has been observed in man (Fig. 5161, *Neu. c*). It might with propriety be termed the canal of Kowalewsky, from its discoverer. Kowalewsky first found it in amphioxus, and subsequently demonstrated its occurrence in various fish types.

The canal lies in front of the true or secondary blastopore and traverses the notochord. According to Durham,[4] it can be well seen in longitudinal sections of early stages of the frog (Fig. 5159) as a short canal, *ne.*, opening widely into the entodermal cavity. Compare also Götte's[7a] description of the neurenteric canal in Bombinator. It was discovered by Gasser[6] in goose embryos. Braun[3] has shown that both canals may be present in various bird embryos at a stage when there are six or eight pairs of myotomes and the development of the tail is just beginning. The neurenteric canal lies a short distance in front of the blastoporic, which is the larger of the two. The two canals appear in some species at the same time, or in other species at slightly different stages. The posterior canal is more often obliterated in birds than the anterior. In the duck and in Motacilla flava the canals are separated both in the times and positions of their occurrence; in the Australian paroquet they are both present contemporaneously, although the neurenteric passage becomes open earliest. Fig. 5160 represents a transverse section, which passes through the neurenteric canal of the paroquet. In the common fowl the blastoporic canal appears not to be open at any period after the formation of the primitive streak.

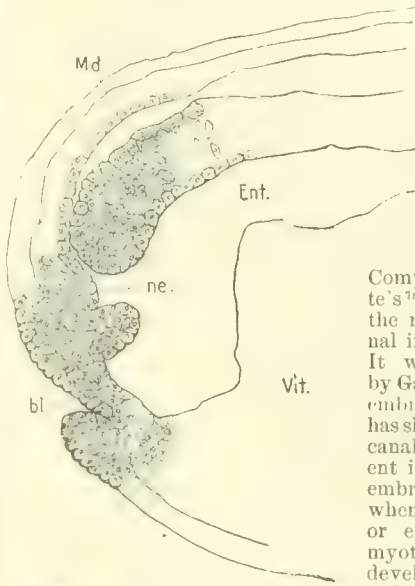

FIG. 5159.—Longitudinal Section of a Frog's Ovum shortly after the Closure of the Medullary Groove. The blastoporic canal, *bl.*, is only partially cut, but was found open in neighboring sections. (After Durham.) *Md.*, Medullary canal; *bl.*, blastopore; *Vit.*, yolk forming the floor of the entodermic cavity, *Ent.*; *ne.*, neurenteric canal.

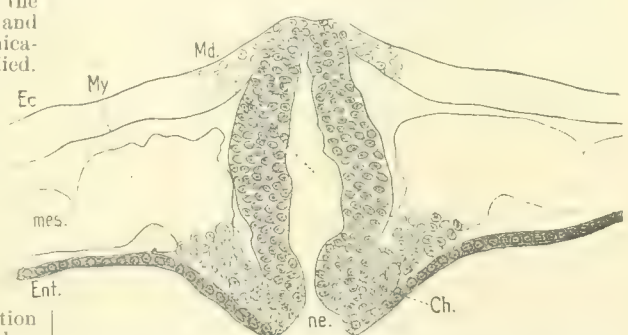

FIG. 5160.—Transverse Section of an Embryo Paroquet (Melopsittacus) to show the Anterior or True Neurenteric Canal. *Ec.*, Ectoderm; *My.* myotome; *Md.*, medullary canal; *Ch.*, notochord pierced by the short neurenteric canal, *ne.*; *Ent.*, entoderm; *mes.*, mesoderm. (After Max Braun.)

Another canal, which was first satisfactorily described by Braun,[3] occurs in older embryos. The "Enddarm" of Gasser and Kölliker becomes the "Schwanzdarm"

(post anal gut, Balfour[1]) of older embryos, which soon becomes divided, at least in birds, into a dilated terminal portion and a narrower neck communicating with the intestine proper. The posterior section then subdivides, and its narrow end segment lengthens out and unites with the spinal cord. This canal we may designate as Braun's canal. It is not improbable that it is homologous with the amnio-allantoic canal of Gasser,[7] which Rauber[12] has nicknamed the Cochin China canal, after the breed of hens in which it seems most constant. In the one case we may suppose the canal to open after, in the other before, the closure of the posterior end of the medullary groove. If the homology is correct it may be further said that the canal is identical with Kupffer's myelo-allantoidean canal; it cannot be brought into relation with the development of the allantois, as believed by Kupffer,[10] as the allantois and Enddarm are both formed before the canal appears.

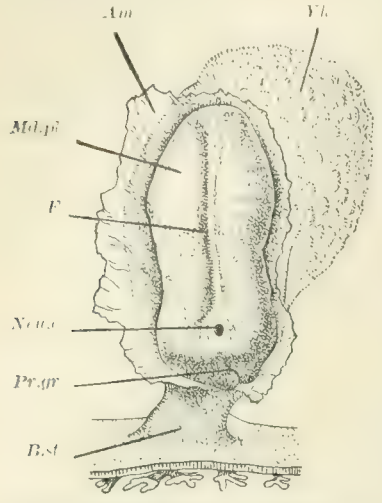

FIG. 5101.—Reconstruction of a Human Embryo 1.54 mm. Long. The amnion has been opened to show the dorsal surface of the embryo. *Yk*, Yolk sac; *Am*, amnion; *Md.pl*, medullary plate; *F*, dorsal furrow; *Neu.c*, neurenteric canal; *Pr.gr*, primitive groove; *B.st*, body stalk. (After Count Spee.) (From Minot's "Embryology," Blakiston, Phila., 1903.)

The significance of the three canals is obscure. The middle one seems unquestionably the temporarily open secondary blastopore. The first, or Gasserian canal, is distinct from the blastoporic, as the two coexist, and it seems desirable that this canal alone should be called *neurenteric*. As to its origin or significance nothing definite can be said, but it may be suggested that it was the excretory opening of the central canal of the spinal cord and that the cilia of the canal served to expel the fluid (compare Balfour[1,2]). This may have been the condition in the earliest vertebrates, and the neurenteric canal now persists as a rudimentary organ. As to the morphological or physiological interpretation of the third or Braun's canal no satisfactory suggestion has been made.

It seems not impossible that a persistent neurenteric canal may occur as an excessively rare anomaly in the adult. *Charles Sedgwick Minot.*

LITERATURE.

The literature of the neurenteric canals is all comparatively recent, and is, for the most part, included in essays dealing with other embryological subjects. Great confusion has arisen from the failure to distinguish the several canals. The reader will find his way most readily by consulting first the text-books of Balfour, [2], [5]; second, the article of Braun,[3]; and third, Rauber's note,[12] although Rauber's terminology is eccentric and perplexing.

[1] Balfour, F. M.: On the Early Development of the Lacertilia, etc. Quart. Journ. Microsc. Sci., xix. (1879): also in his Works, i., p. 644, with Plate 29.

[2] Balfour: Comparative Embryology, vol. ii., pp. 267–269.

Braun, M.: Die Entwickelung des Wellenpapageis: ii. Theil, Semper's Arbeiten, v., 205–341, Taf. x.–xiv. (a valuable but excessively diffuse article. The most important passages on the neurenteric canals are on pp. 296, 301, and 308).

[4] Durham, Herbert E.: Note on the Presence of a Neurenteric Canal in Rana. Quart. Journ. Microsc. Science, xxvi., 509–510, Plate xxvii.

[5] Foster and Balfour: Elements of Embryology, second edition, 1883.

[6] Gasser: Der Primitivstreifen bei Vogel-Embryonen, Cassel, 1879.

[7] Gasser: Beiträge zur Kenntniss der Vogelkeimscheibe. His und Braune's Archiv, 1882, 359–398.

[8] Goette: Entwickelungsgeschichte der Unke.

[8] Heape, Walter: The Early Development of the Mole (Talpa Europa). The formation of the germinal layers, and early development of the medullary groove and notochord. Quart. Journ. Microsc. Sci., xxvi., 1883, 412–452, Plate xxviii.–xxxi.

[9] Hoffmann, C. K.: Die Bildung des Mesoderms, die Anlage der Chorda dorsalis, u. die Entwickelung des Canalis neurentericus bei Vogel-Embryonen, p. 109, 5 Tafeln. Amsterdam, 1883. (Abstr. in Hoffmann u. Schwalbe's Jahresber., 1883, 442–444.)

[10] Kupffer, C.: Die Gastrulation an den meroblastischen Eiern der Wirbelthiere und die Bedeutung des Primitivstreifs. Arch. Anat. u. Physiol., Anat. Abth., 1882, 1–30, Taf. i.–iv. Fortsetzung, 139–156. Taf. viii.–ix.; 2te Fortsetzung, 1883, 1–40, Taf. i.–ii.

[11] Lieberkühn, N.: Ueber die Chorda bei Säugethieren. His und Braune's Archiv, 1882, 399–438, Taf. xx.–xxi. Fortsetzung, 1883, 435–452, Taf. xix.

[12] Rauber, A.: Noch ein Blastoporus. Zool. Anzeiger, vi., 1883, 143–147, and 163–167 (cf. his earlier papers on the Blastoporic Canal, Zool. Anzeiger, ii., 1897, p. 499, and iii., 1880, p. 180).

[13] Strahl: Ueber Canalis neurentericus und Allantois bei Lacerta viridis. His u. Braune's Arch., 1883, 323–340, Taf. xiv.

PERITONITIS.—(Peritonæitis, Inflammatio peritonei.) The peritoneum is a thin membrane of connective tissue extremely rich in blood-vessels and lymphatics, and is covered by a single layer of flattened endothelial (mesothelial) cells (often called epithelial). These cells are chiefly polygonal, but the cell outlines are often very irregular, serrate, or wavy. By treatment with silver nitrate or by *intra vitam* staining with methylene blue, the cement lines between the cells can be made out; and by especial methods of technique the so-called intercellular protoplasmic bridges connecting the cells may be demonstrated. The connective-tissue layer consists of an interlacing network of fibrous connective-tissue bundles, numerous elastic fibres, and connective-tissue cells. Through this there runs a very abundant capillary and lymphatic network having a free anastomosis. The majority of writers hold that the lymphatics communicate directly with the peritoneal cavity by means of small openings between the mesothelial cells, known as stomata. Some of these writers regard the endothelial lining of the lymph spaces of the peritoneal basement membrane as continuous with the lining of the peritoneal cavity. This is not the case, however, and the mesothelial cells form a probably unbroken layer over both the blood and the lymphatic vessels, the processes of absorption and secretion being carried on through the two layers of cells, endothelial and mesothelial. The absorption capacity of the peritoneal surface is very great, being fully equal, in the case of experiments with certain poisons, to that of direct intravenous injections. Gases, fluids, and even morphological elements may be quickly removed from the peritoneal cavity. On the other hand, the secretory activity of the immense vascular surface of the peritoneum is very great, and in disturbances of the vascular secretion an immense amount of exudate may pass through the peritoneum into the peritoneal cavity. The endothelial and connective-tissue cells of the basement membrane respond very quickly to "irritation" of any kind, and fibroblastic activity is set up more quickly in the peritoneum than anywhere else in the body. The course of peritoneal inflammations is considerably modified by these factors.

The peritoneum lines the entire abdominal cavity, and is reflected over the organs contained within it. Over the organs it forms the serous coat or capsule (*tunica serosa*). The membrane is attached to the underlying parts by a subserous coat of adipose tissue, connective-tissue bands and elastic fibres. Over the organs the subserosa is but slightly developed. The anatomical relations of the peritoneum to the abdominal wall, its investiture of the abdominal organs, the intimate relations of the peritoneal cavity to the female genital tract, etc., in connection with its very vascular structure, peculiarly predispose this membrane to the occurrence of inflammatory processes. Such a predisposition is shown by the fact that peritonitis is one of the most common and important clinical conditions. It is also one of the most serious. The high mortality of acute general peritonitis makes it one of the most dreaded affections. Even in these days of aseptic surgery when so many operative procedures have been divested of their chief dangers, peritonitis still remains to the abdominal sur-

geon and gynecologist one of the complications most feared and most carefully to be avoided.

The occurrence of peritonitis is not dependent upon climatic, seasonal, or meteorological influences. Females are more frequently affected than males, this fact being dependent upon the important rôle which diseases of the female genital tract play in the causation of peritonitis. It is therefore seen more often during the years of sexual activity, but may occur at any age. It is of not infrequent occurrence in young children. The relation of peritonitis as a complication to many of the acute infections makes its occurrence to a certain degree associated with epidemics of these diseases. Alcohol is regarded as a predisposing factor.

Etiology.—Peritonitis may be *primary* or *secondary*.

Primary peritonitis is, if we except the surgical form, of much more rare occurrence than the secondary. It is usually *traumatic*, more rarely, *idiopathic*, *spontaneous*, or *rheumatic*.

Traumatic peritonitis is most commonly due to perforating wounds of the abdomen. Abdominal injuries in which the wall is not penetrated rarely, if ever, directly cause peritonitis. Nevertheless, blows, kicks, falls, etc., are often adduced as causes of peritonitis. The more severe the injury, the more likely is the occurrence of peritonitis. Hemorrhage into the peritoneal cavity is usually followed by inflammation of the peritoneum. Likewise, trauma may indirectly cause peritonitis through the perforation, laceration, tearing, or bruising of the stomach or intestines, rupture of the gall bladder, pancreatic duct, urinary bladder, etc., these lesions permitting the entrance of micro-organisms into the peritoneal cavity. The perforation of the œsophagus or stomach by the careless passage of a sound or stomach tube may also be a causal factor in the production of peritonitis.

Operative or *surgical* peritonitis may be mentioned in this connection. Before the days of antisepsis and asepsis a large proportion of laparotomies were fatal from the peritonitis following the operation. Even at the present day the chief anxiety attending operations involving the peritoneal cavity is the possibility of peritonitis. The vast improvement in surgical technique has, however, greatly reduced the number of cases of post-operative peritonitis, and in certain operations in which there is, with proper methods, no opportunity for infection the peritoneal cavity is opened with a certain degree of impunity. The occurrence of surgical peritonitis is dependent upon several factors: the character of the operation and the possibility of infection during the operative procedures, the amount of damage done to the peritoneal tissues, the state of the general resistance of the membrane to infection, etc. Surgical peritonitis is due to the introduction of bacteria into the peritoneal cavity. But not all bacteria which gain an entrance into the peritoneal cavity set up an inflammation there. It has been shown experimentally that rather large quantities of bacteria, even of the pus cocci, may be introduced into the peritoneal cavity of animals without causing peritonitis, the bacteria entirely disappearing after a short time. The presence of a tissue lesion, even though very slight, or the simultaneous introduction into the cavity of irritating substances, furnishes the conditions requisite for the growth of the bacteria and for the production of an inflammation. The peritoneum therefore when uninjured must possess a certain protective power against bacteria. This resistance is found to be lowered in the case of hemorrhage into the cavity, after the removal of ascitic fluid, and in cases of pseudomyxoma peritonei. The general condition of the body, conditions of intoxication, cachexia, etc., also play a rôle of importance. Fatal peritonitis may follow the tapping of the abdomen in ascites, the small number of bacteria introduced by means of a septic trocar being sufficient to overcome the lessened resistance. When modern methods of asepsis are properly carried out the dangers of surgical peritonitis are relatively slight in all cases in which the contamination of the peritoneum with septic material can be avoided. Even when this contamination does occur, the modern procedures of thorough irrigation have greatly reduced the chances of infection.

The existence of a *peritonitis rheumatica* (*refrigeratoria*) has been denied by many writers. While the effects of cold as a factor in the etiology of peritonitis were formerly greatly exaggerated, there can be no doubt, from the large number of observations made by reputable clinicians, that attacks of peritonitis may follow the sudden chilling of the overheated body, prolonged exposure to cold or wet, lying upon the cold damp ground, etc. The effects of such chilling of the body are especially noticeable when the abdominal vessels are overfilled with blood (*physiological congestion*). In women, particularly in girls at the time of puberty, a wetting or chilling of the body at the menstrual period is not infrequently followed by peritonitis. In all of these cases the effect of the refrigeration is not directly to excite the peritonitis, but to render the membrane less resistant to infection. The chilling plays the same rôle here as in the case of the mucous membranes. Diplococci have been demonstrated in the exudate of cases of so-called rheumatic peritonitis; and it is very probable that all such cases are infections following and dependent upon a lessened resistance of the body.

Cases of *idiopathic* or *spontaneous* peritonitis have also been reported clinically.

The autopsy findings in such cases show the presence of an infection proceeding from the female genital tract, the appendix, or some other of the abdominal organs. Such cases occur most frequently in females and in very young persons. In the former the infection is nearly always secondary to some unsuspected condition of the internal genitals. The gonococcus plays an important rôle in such cases, particularly in very young girls. It has been said that the peritonitis apparently arising spontaneously in young girls is usually gonococcal, a gonorrhœal infection of the genital passages existing at the same time. In young male children cases of apparent spontaneous peritonitis are usually found to be due to appendicitis. Further, spontaneous cases of peritonitis have been found at autopsy to be ambulatory typhoid, acute tuberculosis of the peritoneum, etc. On the whole it may be said that the existence of a true idiopathic peritonitis, while probable, has not yet been definitely demonstrated. A *cryptogenic hæmatogenous* infection of the peritoneum is of course possible and certainly occurs in tuberculous peritonitis, but has not yet been shown positively to occur in the case of the pyogenic organisms.

Likewise the existence of a toxic peritonitis, though assumed by some writers, has not been demonstrated. The occurrence of so-called *nephritic* or *uræmic* peritonitis seen in the late stages of Bright's disease is to be regarded as of the nature of a terminal infection, and similar to the pericarditis and pleuritis occurring in the same disease. The occurrence of peritonitis in association with or following various forms of intoxication is to be explained in the same way as the rheumatic—the lessened resistance of the body tissues and the pathological alterations of the body juices predispose to infection.

Since primary inflammations of the pericardium and pleura are of relatively more frequent occurrence, the greater rarity of primary peritonitis may be explained by the assumption that the peritoneum possesses a greater resistance and protective power than the other serous membranes. This relative greater immunity of the peritoneal cavity has been demonstrated experimentally.

Secondary Peritonitis.—It should be noted at this point that various writers upon the subject of peritonitis are not agreed in their conceptions of primary and secondary peritonitis. In a very broad sense the term primary may be applied to those forms of peritonitis which are not secondary to, or do not occur in association with, any other acute or chronic disease, hence not metastatic; and, further, which do not arise by contiguity from any of the organs or structures covered by the peritoneum. Terminal infections should then be classed as secondary rather than as primary. A number of recent

writers, notably Flexner, in retaining the old classification of primary and secondary peritonitis, make a much narrower application of the term *secondary* as applying to peritonitis. According to Flexner, by *secondary* peritonitis we should understand those conditions which follow operations upon the peritoneum or the contiguous viscera, and those in which the abdominal cavity becomes inflamed through the mediation of disease-contained viscera. By *primary* peritonitis should be understood an inflammation, usually diffuse, of the serous cavity, occurring without the mediation of any of the contained organs and independently of any surgical operation upon these parts. Such a primary peritonitis may arise as an independent affection or develop in the course of infectious diseases in distant parts of the body. The micro-organisms causing the inflammation may be brought by the blood or lymph current or may pass through the intact intestinal wall. Flexner would therefore class as primary not only the terminal infections of the peritoneum occurring in the course of chronic diseases, but also those forms of metastatic peritonitis in which the micro-organisms come through the blood or lymph without the mediation of some diseased organ or part. The reason given for this more arbitrary and narrower use of the term secondary and the wider application of the term primary is that pathogenic micro-organisms may reach the healthy peritoneum without setting up an inflammation, but that "only an already inflamed peritoneum can be excited to peritonitis through the agency of pathogenic micro-organisms." Used in this way the terms primary and secondary indicate the character of the affection rather than the source of the cause or the manner in which the peritonitis arises. Since such a usage may be confusing, the writer has preferred to adhere to the more commonly accepted use of the terms as given above, viz., *primary peritonitis*, an inflammation of the peritoneum arising primarily and independently of other processes, as the result of chemical or mechanical irritation or as a direct or cryptogenic infection, or as the result of a lessened resistance of the peritoneum due to trauma, toxic conditions, or altered conditions of the peritoneum caused by foreign bodies, presence of fluid, etc., analogous to primary infections in other parts of the body; *secondary peritonitis*, an inflammation of the peritoneum, secondary to some other process, arising by contiguity or metastasis, or occurring as a terminal infection. Even with this broader standard of classification no hard-and-fast lines can be drawn. Inasmuch as cases of primary peritonitis are rare, and as the peritoneum possesses a normal resistance against pathogenic micro-organisms, practically all cases of peritonitis are secondary.

In the great majority of cases secondary peritonitis arises through an *extension* of an inflammatory process from some contiguous viscus or part. There is no organ or tissue in direct contact with the peritoneum from which such an extension may not occur. The possibilities are so numerous that it is necessary to refer here only to the most common or important. The extension to the peritoneum may or may not be accompanied by perforation into the peritoneal cavity. In the latter case the resulting inflammation is known as a perforative peritonitis.

Perforative Peritonitis.—This is the most common form of secondary peritonitis. It may result from the perforation into the peritoneal cavity of an infected wound of the abdominal wall or of a viscus (traumatic or operative), or from the perforation, as the result of inflammatory processes, of the wall of the stomach, intestine, gall bladder, pancreatic duct, urinary bladder, uterus, tubes, blood-vessels, lymph vessels, etc. Abscesses of the abdominal viscera, echinococcus cysts, tumors, burrowing suppurative processes in the retroperitoneal tissues, etc., may also give rise to perforative peritonitis. It is hardly expedient to enumerate here all the possibilities whereby a perforative peritonitis may arise, and only those of greatest clinical importance will be mentioned.

In the case of the *stomach* perforative peritonitis may be caused by carcinoma, gastric ulcer, abscess, phlegmonous gastritis, action of corrosives, foreign bodies, etc. In the *intestines* ulcers (typhoid, dysenteric, catarrhal, tuberculous, syphilitic, carcinomatous, etc.), new growths, foreign bodies, parasites, gall stones, fæcal concretions, fæcal obstruction, intussusception, ileus, hernial incarceration, etc., may lead to perforative peritonitis. Perforation of a suppurating *appendix* is one of the most common causes of peritonitis.

In the case of the *spleen* perforative peritonitis may be caused by splenic infarcts, abscesses, echinococcus cysts acute splenic tumor leading to rupture of the organ, rupture of a dilated splenic vein, metastatic tumors, etc. In the *liver* the same condition may result from abscesses, echinococcus cysts, rupture of bile passages, biliary concretions, new growths, etc. Rupture of the *gall bladder* or *common duct*, ulcerative processes in the walls of the gall bladder or ducts, presence in these of concretions, etc., may likewise lead to perforative peritonitis. This may be caused also by pancreatic concretions, abscesses and tumors of the *pancreas*, hemorrhagic and purulent pancreatitis, etc. Fat necrosis may or may not be associated with the peritonitis dependent upon pancreatic conditions.

Perforative peritonitis may also arise in connection with abscesses and tumors of the *kidneys* or *adrenals*, kidney tubercles, echinococcus cysts, renal calculi, purulent pyelitis, peri- and paranephritic abscesses, etc. Ulcerative and phlegmonous processes of the *urinary bladder*, new growths of the bladder, cancer of the *uterus*, purulent and gangrenous conditions of the uterine wall, purulent salpingitis, tubal pregnancy, tubo-ovarian abscess, ovarian tumors, rupture of Graafian follicle and ovarian cysts, suppurative processes of the retroperitoneal and mesenteric lymph glands, thrombophlebitis, and thrombo-arteritis of the abdominal vessels, rupture of abdominal aneurisms, rupture of the thoracic duct or dilated lymphatics, subperitoneal tumors and abscesses, psoas abscess, carious and purulent processes in the spinal column and pelvic bones, etc., may all lead to perforative peritonitis. In rare cases purulent processes proceeding from the mediastinum, pleura, pericardium, lungs, diaphragm, thoracic vertebræ, etc., may rupture into the peritoneal cavity and there excite an inflammation.

In the case of perforative peritonitis there will be found in the peritoneal cavity, in addition to the inflammatory exudate, various substances of very different nature according to the location of the perforation and the character of the contents of the cavity communicating with the peritoneal sac. Stomach contents, fæces, fæcal concretions, bile, biliary concretions, pancreatic juice, urine, urinary calculi, foreign bodies, parasites, blood, chyle, mucin, pseudomucin, colloid, etc., may be mixed with the exudate. According to the character and amount of the substances thus entering the cavity, and according to the character and amount of the peritoneal exudate the appearances seen at operation or autopsy will differ greatly.

Some writers distinguish a *secondary perforative peritonitis*, grouping under this head those conditions in which the exudate of a purulent peritonitis, originally not perforative, gains entrance to some neighboring organ, and through it finds an exit, as, for example, through the stomach, intestine, pleura, abdominal wall, etc. Such cases should more properly be styled *perforating peritonitis*.

Peritonitis Arising by Contiguity.—Peritonitis may arise secondarily by the direct extension of inflammation caused primarily by wounds (operative or traumatic) of the abdominal or pelvic wall, gastric ulcer, gastric cancer, phlegmonous gastritis, toxic gastritis, duodenal ulcer, intestinal ulceration (typhoid, dysenteric, catarrhal, tuberculous, syphilitic, carcinomatous), new growths of the intestine, coprostasis, intussusception, ileus, hernial incarceration, presence of intestinal concretions, parasites and foreign bodies, typhlitis, appendicitis, proctitis, liver abscess, new growths of liver, hepatitis, angiocholitis, inflammatory processes due to echinococcus, biliary

concretions, etc., pancreatitis, pancreatic abscesses and presence of pancreatic concretions, splenic abscess and infarction, hydatid disease of spleen, kidney abscess, peri- and paranephritic abscesses, inflammatory processes caused by renal calculi, pyelitis, ureteritis, cystitis, inflammations of ovary, tubes, uterus, vagina, prostate, retroperitoneal or mesenteric glands, psoas abscess, congestive abscesses of spinal column or pelvic bones, inflammations of abdominal or pelvic vessels, suppurating buboes in the inguinal region, inflammatory processes of the mediastinum, œsophagus, pleura, pericardium and diaphragm, etc. In the case of inflammatory processes in the pleural cavity (tuberculous, empyema, etc.) the peritoneum is not infrequently involved, inasmuch as the lymph vessels of the diaphragm form a direct connection between the pleural and peritoneal cavities.

Next to the gastro-intestinal tract the *female genital tract* is the most frequent source of peritoneal infection. In women genital peritonitis is by far the most common form of the affection. During the puerperium or as the result of attempts at abortion, operative procedures, intra-uterine injections, etc., the genital tract may be directly infected; less frequently the infection occurs at other times, as for instance at the menstrual period. The resulting endometritis, metritis, parametritis or salpingitis may extend to the peritoneum and excite peritonitis. Purulent processes of the endometrium may extend directly up the Fallopian tubes. In other cases the extension of purulent processes from the vagina or uterus may take place through the lymphatics or blood-vessels. Large abscesses of the uterine wall or tube may break directly into the peritoneal cavity. Further, cases of apparently primary peritonitis have been reported as occurring in pregnancy without any association with rupture of the uterus or other complications of pregnancy. The discovery at autopsy of the existence of extensive renal changes makes it probable that such cases of peritonitis are secondary to the nephritis.

Gonorrhœa of the female genital tract is also an important factor in the production of peritonitis (see below). It must be noted further that in many cases of septic puerperal peritonitis the uterus and tubes serve as avenues of entrance to the agents of infection while remaining themselves in a normal condition.

An especial factor in the production of peritonitis of the female genital tract is that offered by the twisting of the pedicles of ovarian cystomata or of subserous uterine myofibromata. As a result of the shutting off of the circulation from the tumor, the tissues of the latter undergo necrosis, and the necrotic material offers a most favorable field for infection, particularly from the intestine. Such infections are very likely to result in a gangrenous peritonitis. In case infection of the dead tumor tissue does not occur a non-infectious peritonitis may result, the dead tumor acting as an irritating foreign body. A very virulent peritonitis may be thus excited, the exudate as well as the necrotic tumor containing no micro-organisms. Dermoid cysts appear to be especially susceptible to infection after twisting of their pedicles.

The rupture of an uninfected ovarian cystoma and the discharge of a thin serous fluid into the peritoneal cavity rarely excite a peritonitis, the fluid being quickly absorbed. The absorption power of the peritoneum under such circumstances is very great. Only those cystomata containing a firm jelly-like substance (mucin, pseudomucin, colloid) are dangerous, since the cyst contents cannot be easily absorbed and act upon the peritoneum as foreign bodies, leading to an organization and vascularization of the material (aseptic peritonitis, pseudomyxoma peritonei). It should be remembered, however, that in such cases secondary peritonitis is very likely to occur owing to the diminished resistance of the peritoneum; consequently a combination of pseudomyxoma and an acute or subacute peritonitis is not infrequent. Operation with the removal of the jelly-like cyst contents from the peritoneal surface after organization has begun is especially likely to be followed by infection of the raw surface thus exposed. In the case of the rupture of cysts containing chemically irritating material (*pancreatic cysts, chyle cysts*), a non-infectious, acute, and very virulent peritonitis may be set up.

Secondary peritonitis is also not infrequently associated with metastatic carcinoma (*peritonitis carcinomatosa*) and tuberculosis of the peritoneum (*peritonitis tuberculosa*). These conditions will be discussed below.

In the *acute infections* peritonitis is occasionally met with as a complication. In *septicæmia* and *pyæmia* peritonitis is a very frequent complication. It occurs less often in *pneumonia, smallpox, varicella, measles, scarlet fever, diphtheria, erysipelas, malaria, relapsing fever*, etc. From the increasing number of cases reported *pneumonia* seems to be somewhat particularly associated with peritonitis, and the pneumococcus has recently been found in the peritoneal exudate of a number of cases. The peritonitis may be secondary to the pulmonary symptoms or may appear to be the primary condition, the peritonitis manifesting itself before the pulmonary affection. It is probable that such cases represent a general infection by the pneumococcus, the localization varying in different cases. They may therefore be classed as *peritonitic pneumonia*, in analogy to the types known as cerebral and gastric. Pneumococcic peritonitis may also be secondary to pneumococcic pericarditis, empyema, and arthritis. The occurrence in various parts of the body of multiple metastatic abscesses containing peumococci is evidence of the pyæmic nature of the process.

According to Bednar peritonitis may develop after *vaccination*.

Metastatic peritonitis occurs in *malignant endocarditis* and in *pyæmia*. The primary focus may occur in any part of the body, and may be of very slight extent. Peritonitis has followed the infection of a circumcision wound, and very slight lesions in other parts of the body have led to the same fatal termination. It is not uncommon in such cases to find all the serous membranes involved—an acute panserositis; meningitis, pleuritis, pericarditis, and arthritis as well as peritonitis. Peritonitis may also develop during the course of *acute articular rheumatism*. The exact relation of the two conditions is unknown; the peritoneal inflammation is either metastatic or dependent upon a lessened resistance of the membrane to cryptogenic infections. Likewise acute peritonitis is sometimes associated with *acute nephritis*. It is possible that in these cases the intoxication plays some part in the development of the process, most probably by lowering the resistance of the membrane. The exudate in these cases is usually serous, and bacteria cannot always be obtained from it by culture methods; hence some writers regard these forms of peritonitis as of chemical origin and primary.

Terminal Peritonitis.—Peritonitis also occurs not infrequently as a terminal infection in chronic valvular disease, arteriosclerosis, chronic nephritis, cirrhosis of the liver, amyloid disease, tumor cachexia, scorbutus, etc. The peritoneum alone of the serous membranes may be affected, or the pericardium and the pleura may also become inflamed. Micro-organisms are usually present in the exudate. In those cases in which they are not found it is possible that they were present earlier in the disease, and later disappeared. It is of course possible that the peritonitis in some of these cases may be toxic or chemical, but it is more likely that the general intoxication has lowered the resistance of the membrane and cryptogenic infection has occurred.

There is also a close relationship between *syphilis* and peritonitis. Acute peritonitis not infrequently develops in the early stages of acquired syphilis, but is usually a secondary infection. It is not known whether an actual syphilitic peritonitis exists, though it is very probable that it does, inasmuch as a so-called idiopathic peritonitis is of common occurrence in syphilitic new-born. In the tertiary stage of acquired syphilis evidences of local peritonitis are common enough at autopsy. Chronic perihepatitis and chronic perisplenitis are more common in syphilitics than in non-syphilitics.

Foreign bodies (concretions, parasites, forceps, needles,

hairs, etc.) when aseptic produce a local encapsulating peritonitis. When septic they may excite a diffuse purulent or fibrinous process. Free bodies, such as fat tissue, blood clots, pieces of fibroid tumors, etc., may become calcified or encapsulated, setting up a local adhesive peritonitis. In *extra-uterine pregnancy* hemorrhage into the peritoneal cavity following the rupture of the sac may excite an intense peritoneal irritation even in the absence of infection. In such cases the blood itself must exert a chemical irritation upon the peritoneum, or irritating toxins are contained or developed within it.

Finally, during *extra-uterine injections* irritating substances may be forced through the tubes into the peritoneal cavity and excite a toxic inflammation. Such cases may occasionally be properly classed with the primary forms of peritonitis, but inasmuch as some inflammatory condition of the uterus or tubes is usually present it becomes difficult to say to what extent the injection is alone responsible for the peritonitis.

Parasites.—A number of observers have noted at autopsy the presence, in the peritoneal cavity, of intestinal worms in association with a perforative peritonitis. In some cases the perforation has been regarded as caused by the parasite (usually the common round worm), the peritonitis following the perforation. Some of the reported cases are very doubtful. Katsurado several years ago reported two cases of purulent peritonitis which he regarded as caused by round worms. A very careful examination, both at the time of operation and at the autopsy, failed to reveal any other cause for the peritonitis. In both cases the affection ran a very severe course. Osler and other recent writers accept the view that *Ascaris lumbricoides* may penetrate the intestinal wall and excite peritonitis. The *Amœba coli* has been found in the exudate of peritonitis.

Under rare conditions peritonitis may follow other conditions not mentioned above. As stated before it is hardly feasible to enumerate all the possibilities, but the most common and important sources of secondary peritonitis have been given; and if the extensive anatomical relations of the membrane are borne in mind it will usually not be difficult to trace to its source any secondary peritonitis that may be encountered.

Bacteriology.—Inasmuch as the great majority of cases of peritonitis are caused by bacteria the bacteriology of peritonitis becomes a matter of very great importance. In recent years a number of important investigations have been carried out along this line, but much work yet remains to be done before we shall possess a fully satisfactory knowledge of the subject. It has been demonstrated that very different forms of bacteria may be found in the exudate of peritonitis. In the majority of cases there is a mixed infection, several varieties of pathogenic bacteria being present, or a number of varieties of pathogenic and non-pathogenic bacteria may be found together. According to Tavel and Lanz the hæmatogenous cases of peritonitis are mono-infections, while those arising by contiguity from a neighboring diseased organ are usually poly-infections. It is probable that in some at least of the cases of mono-infection the single variety found may have crowded out other varieties which were originally present. This is particularly likely to have been the case in those instances in which the only micro-organism present is a harmless saprophyte. In those cases in which the exudate is sterile there is also the possibility that the original pathogenic bacteria causing the inflammation have died out.

The pathogenic bacteria most frequently found in peritonitis are the *Streptococcus pyogenes*, *Staphylococcus aureus*, *Staphylococcus albus*, *Bacterium coli commune*, *Diplococcus pneumoniæ*, *Bacillus pyocyaneus*, and the *Gonococcus*. (Tuberculosis of the peritoneum will be considered separately.) Less frequently found are the *Bacillus typhosus*, *Bacillus aerogenes capsulatus*, *Bacillus proteus*, *Bacillus lactis aerogenes*, *Micrococcus tetragenus*, and a number of unidentified pathogenic and non-pathogenic bacteria.

In perforative peritonitis the *Bacillus coli communis* usually predominates; in puerperal peritonitis the chief rôle is played by the *Streptococcus pyogenes*; while in those cases of peritonitis which apparently arise spontaneously the *Pneumococcus* or the *Gonococcus* is the chief exciting factor. In all those cases of peritonitis in which the infection comes from without the flora resembles that of ordinary surgical infections, except for the prominent part played by the colon bacillus. In those cases which arise by contiguity from some one of the neighboring organs the staphylococcus plays a chief rôle, except in the case of intestinal infection in which the colon bacillus alone or combined with the former is usually found.

Much discussion has taken place as to the pathogenic rôle of the colon bacillus in peritonitis. The pyogenic properties of this organism have been quite generally accepted, and there can be no doubt of the existence of a primary colon-bacillus peritonitis. In the majority of cases in which the colon bacillus is found pyogenic cocci are also present, and it is probable that in some of the instances in which this organism alone was found in the exudate it had overgrown the cocci. Barbacci in experimental work upon dogs found that the colon bacillus often outgrew the pyogenic cocci. Infections of the peritoneum with the colon bacillus occur through the bladder and female genital tract as well as directly from the intestine. There are still several questions to be settled before the exact pathogenic value of the colon bacillus can be fixed. Its relations to the pyogenic cocci need to be more definitely determined in regard to the part played by each as primary excitants of inflammation. Further, many of the cases regarded as colon-bacillus infections were diagnosed as such from the results of the bacteriological examination made at autopsy some hours after death. As the colon bacillus may enter the peritoneal cavity after death and increase there, overgrowing other bacteria, it is necessary, in order definitely to determine the relation of this organism to a peritonitis, to make bacteriological examinations of the peritoneal exudate during life.

An effort has been made by a number of writers to make a bacteriological classification of peritonitis. Freund divided all cases of peritonitis into three classes: one due to pyogenic organisms, one to fæcal bacteria, and the third to toxic substances. Bumm distinguished a septic, aseptic, and a specific peritonitis. The septic he divided into a streptococcus peritonitis and a putrid peritonitis, the latter not caused by any one form of bacteria but by a multiple infection. The aseptic peritonitis he regarded as due to mechanical, thermal, or chemical influences alone without bacterial agency. In the class of specific peritonitis he placed tuberculous and gonorrhœal peritonitis. Tavel and Lanz have offered a more complex classification based upon the anatomical origin of the infection, special kinds of peritoneal infection being derived from the stomach and intestine, the gall bladder and liver, the female genital tract, the kidneys, urinary bladder, etc., other forms still being derived from hæmatogenous infections and operations.

Flexner has reported a series of observations upon one hundred and six cases of peritonitis studied from the bacteriological point of view. The material was obtained at autopsy, cover-glass and aërobic cultures being carried out. Few anaërobic cultures were made and the pathogenic properties of the bacteria isolated were tested but rarely. In spite of this incompleteness of the investigation the results are of interest. Twelve of the cases presented the character of a primary peritonitis according to Flexner's definition. In all these cases there was a previous chronic disease. In two cases no micro-organisms were found; in nine cases there was a single infection, and in one case a multiple infection. The *Streptococcus pyogenes* was found five times, four times alone, and once in association with the colon bacillus; the *Staphylococcus aureus* and *albus* twice, the *Micrococcus lanceolatus*, *Bacillus proteus*, *Bacillus pyocyaneus*, and an unidentified bacillus occurred twice each.

The secondary cases Flexner divides into two classes: *exogenous* peritonitis and *endogenous* peritonitis. In the

former the infection entered from without (wound infection), in the latter the bacteria came in part or wholly from the intestinal tract. Thirty-four cases of the exogenous form were examined. Of these, 25 were monoinfections, nine were multiple. The following tables are taken from Flexner's article (Philadelphia *Medical Journal*, 1898):

MICRO-ORGANISMS FOUND IN CASES OF EXOGENOUS PERITONITIS

	Total number of cases	Alone.	Combined.
Staphylococcus aureus	16	12	4
Staphylococcus albus	7	2	5
Streptococcus pyogenes	10	5	5
Bacillus coli communis	7	2	5
Micrococcus lanceolatus	3	1	2
Bacillus proteus	1	0	1
Bacillus pyocyaneus	2	1	1
Unidentified organisms	3	1	2

COMBINATIONS.	Number of cases.
Staphylococcus aureus and Streptococcus	1
Staphylococcus albus and Streptococcus	1
Staphylococcus albus and Bacillus proteus	1
Staphylococcus albus and Bacillus coli communis	1
Streptococcus and Bacillus coli communis	1
Streptococcus, Bacillus pyocyaneus and Coli communis	1
Streptococcus and Bacillus pyocyaneus	1
Micrococcus lanceolatus and Bacillus coli communis	1
Micrococcus lanceolatus and lique fying bacillus	1

Of 60 cases of endogenous peritonitis 58 gave positive bacteriological results. Single infections occurred in 21 cases of these, and multiple infections in 37.

BACTERIA FOUND IN CASES OF ENDOGENOUS PERITONITIS

	Number of cases.	Alone.	Combined.
Bacillus coli communis	15	9	38
Streptococcus pyogenes	39	7	32
Staphylococcus albus	4	2	2
Staphylococcus aureus	3	1	2
Micrococcus lanceolatus	4	1	3
Bacillus proteus	4	2	2
Bacillus aerogenes capsulatus	8	2	6
Bacillus pyocyaneus	3	0	3
Bacillus typhosus	3	0	3
Unidentified	3	0	3

COMBINATIONS.	Number of times.
Streptococcus and Bacillus coli communis	16
Streptococcus, Bacillus aerogenes, and Bacillus coli	2
Streptococcus and Bacillus aerogenes capsulatus	1
Streptococcus and Staphylococcus aureus	1
Streptococcus and Bacillus typhosus	2
Streptococcus and Staphylococcus aureus, Bacillus typhi, proteus and coli	1
Streptococcus and Bacillus proteus	1
Streptococcus and unidentified organism	1
Bacillus coli and Micrococcus lanceolatus	3
Bacillus coli and Bacillus pyocyaneus	3
Bacillus coli and Bacillus aërogenes capsulatus	2
Bacillus coli, Staphylococcus aureus, and Bacillus aërogenes capsulatus	1
Staphylococcus albus and orange sarcina	1
Staphylococcus albus and unidentified organism	1

The comparison of the table in the exogenous and endogenous forms is of interest. It will be seen that multiple infections are relatively more frequent with the endogenous form, and that the variety of bacteria is much greater. The streptococcus takes the place which the staphylococcus holds in the exogenous cases and the colon bacillus plays a much more important rôle. The small part which the pathogenic staphylococci seem to play in endogenous peritonitis is of clinical importance, inasmuch as the streptococcic infections may be associated with metastasis. The infections in the exogenous cases resemble those of ordinary surgical or traumatic infections. Basing his conclusions upon the observations, Flexner would distinguish three forms of peritonitis: a primary or idiopathic form restricted to a small number of terminal infections; a second variety analogous to surgical infections; and a third variety dependent upon disease of an intraperitoneal organ, whereby micro-organisms and other extraneous substances gain entrance to the peritoneal cavity, break down its resistance, and lead to infection.

Pneumococcic Peritonitis.—Cases of peritonitis due to the *pneumococcus* have been described by Frotscher, Fraenkel, Charrier, Veillon, Beco, Bryant, Comby, Brun, Burckhard, and others. Brun reports fourteen cases of pneumococcus peritonitis in children. The majority of the cases of peritoneal infection with the pneumococcus occur in young girls. The avenue of infection is through the genital tract. The peritonitis may or may not be associated with inflammations of other serous membranes. The infection is frequently localized in the pelvis. The prognosis is favorable in those cases in which the exudate becomes encysted by adhesions, but metastases and localizations of the micro-organism in other parts of the body may occur. The diffuse form is usually fatal. In the case of operative procedures in pneumococcus pyosalpinx the greatest care must be taken to prevent infection of the peritoneum since the peritonitis thus excited is usually very virulent. Pneumococcus peritonitis may also result from extension or perforation in the case of a pneumococcus appendicitis. The relation to pneumonia and arthritis has been mentioned above. It is of importance in the diagnosis of this condition to bear in mind the fact that after death the pneumococci may entirely disappear from the peritoneal exudate, the colon bacillus or some other organism being left. Cases have been reported in which the examination of the pus from the peritoneal cavity during life, or soon after death, showed the presence of pneumococci in great numbers, while examinations made twenty-six to forty-eight hours later showed only the presence of intestinal bacteria.

Gonorrhœal Peritonitis.—The occurrence of an acute general peritonitis caused by the *Gonococcus* is now firmly established, and the condition is probably not infrequent in women affected with gonorrhœa of the internal genitals. Wertheim in opposition to Bumm was the first to maintain that gonococci may multiply within the peritoneal cavity and excite there an inflammation which may spread over the entire peritoneum. An increasing number of such cases is being reported. The view of Bumm and others, that the *Gonococcus* finds no favorable soil upon serous surfaces, and that its growth upon the peritoneum is slight and localized has been completely overthrown by recently reported cases. The infection of the peritoneum with the *Gonococcus* occurs chiefly in women, although cases of gonorrhœal peritonitis in men have been reported by Jadassohn, Horowitz, von Zeissl, and others. In the female the infection usually proceeds from the tubes. In the case of an infection of the woman with very virulent gonococci there may develop suddenly a most severe general peritonitis. The passage into the peritoneal cavity, from the mouth of the tube, of pus rich in gonococci always excites a general peritonitis; if the flow is small, and if but few gonococci are present in the pus, or if these are reduced in virulence a local peritonitis is usually set up. Gonococcic peritonitis is relatively more frequently a complication of gonorrhœal vaginitis and vulvitis in young girls. Such cases are unfortunately not rare in some of our large cities. The belief held by certain of the lower classes that gonorrhœa in the adult may be cured by rubbing the male organ over the external genitals of young girls is probably responsible for some of these cases. The peritoneal affection may appear as a mild or severe acute general peritonitis, or it may run a latent course as a chronic inflammation. The prognosis in these cases is always serious. Recovery may be followed by sterility.

PATHOLOGY.—The pathological changes found in the peritoneum in inflammation of this membrane are essentially the same as those occurring in inflammatory processes of the pleura and pericardium. According to the duration of the inflammation there may be distinguished an *acute*, *subacute*, or *chronic* peritonitis. According to the extent of the membrane involved a peritonitis may be

local or *circumscribed*, *general* or *diffuse*. A localization of the inflammation in the pelvis is generally spoken of as a *pelvic* peritonitis, in the neighborhood of the appendix as *peri-appendicial*, over the spleen and liver as *perisplenitis*, *perihepatitis*, etc. According to the nature of the exudate there may be distinguished a *serous*, *fibrinous*, *purulent*, *hemorrhagic*, and a *putrid* or *gangrenous* peritonitis. Besides these pure types a variety of combinations, such as sero-fibrinous, sero-purulent, fibrino-purulent, sero-hemorrhagic, etc., occur.

Within certain limits the anatomical picture presented in all cases of peritonitis is essentially the same, but the appearances seen at autopsy or operation may vary greatly according to the chronicity, severity, and extent of the inflammation, the amount and character of the exudate, etc. The picture of a severe *acute general peritonitis* is, however, very characteristic. The abdomen is distended and tympanitic over the dome and dull over the flanks. When the cavity is opened the distended coils of intestine rise up through the opening, and an escape of gas may take place, even in non-perforative peritonitis. The serous surfaces are cloudy, in slight cases having the appearance of glass which has been breathed upon. Both the parietal peritoneum and the outer surface of the coils may be more or less reddened, injected, or even show ecchymoses. When the coils are lifted up and separated the reddened areas appear to be arranged in bands along the intestine. As a rule these reddened bands correspond to the spaces between the coils at those places at which the sides of the coils do not touch. The vessels of the serosa of these spaces are usually markedly hyperæmic, while at those points at which the coils do touch the vessels are less congested. According to Wilks and Moxon these spaces, which are triangular on cross section, form a system of communicating tubes through which the exudate may spread; and because of the lower resistance over these free surfaces absorption of the exudate is carried on here to a greater extent than elsewhere over the peritoneal surface. The loss of lustre and the cloudiness of the serous surfaces are due partly to the degeneration and desquamation of the endothelium, and partly to a layer of fibrin which is deposited over the surface. The latter may vary greatly in amount; in some cases the fibrin film may be so thin that it can be seen only as a slight cloudiness when examined by oblique light, or it may be made evident by rubbing off the delicate coating with a damp cloth or by scratching the serosa with the edge of the knife. In other cases the serosa may be covered with a thick, grayish, yellowish, yellowish-gray or reddish-gray exudate which may extend over the coils in a sheet, or in strings or bands of varying size, or appear as flakes scattered over the dull, lustreless surface. The fibrin may bind the coils more or less firmly together; in acute cases such adhesions are easily separated by the fingers, but in older cases the adhesions become organized to a greater or less extent, and so firm that they cannot be torn. The spleen and liver may become entirely covered by fibrinous sheets, or tags and flakes of fibrin may be scattered over their capsules. The amount of fibrin may be much greater in some parts of the cavity than in others, and by causing adhesions between neighboring structures may shut off portions of the cavity and confine the fluid exudate to certain regions.

Free fluid is usually present in the dependent portions of the cavity, in the flanks, pelvis, and the pockets between the coils. The amount varies greatly, sometimes many litres (20–40) causing a great distention of the abdomen, while at other times only a small amount is present. The fluid is always more or less cloudy or opaque, but varies in character according to the nature of the exudate, the character of the infection, the occurrence of perforation, etc. It may be serous, purulent, hemorrhagic, fibrinous, putrid, etc. In the great majority of cases it is fibrino-purulent, a pure purulent character rarely occurring, although a purulent character usually predominates. Rarely is it serous or sero-purulent. It is very often putrid (perforative peritonitis), and is then sanious, greenish, or grayish, having a gangrenous odor, and may contain gas bubbles. Except in the case of tuberculosis or carcinoma a hemorrhagic exudate is very rare. The distribution of the exudate is generally very irregular owing to fibrinous adhesions. It usually collects in greatest amounts in the pelvis, flanks, splenic and hepatic regions, and in the deeper parts of the two hypochondriac regions. It often becomes encapsulated by fibrinous adhesions between the coils themselves, or between these and the abdominal wall or some one of the abdominal organs. The omentum often plays an important part in the encapsulation of exudates of small size in the appendix region and in the neighborhood of perforating ulcers of the intestine. Large collections of exudate are often found between the liver and the diaphragm; when of a purulent character and encapsulated from the other portions of the cavity the condition is often spoken of as a *subdiaphragmatic abscess*. Gas is particularly likely to collect in this region. In some cases the liver may be pressed tightly against the diaphragm, its diaphragmatic surface flattened and dry. The exudate often follows along the tubular spaces between the coils, so that the exudate from a pelvic peritonitis may pass under the lower coils of the ileum into the cæcal region and upward along the ascending colon to the right hypochondrium, then along the lesser curvature of the stomach to the cardiac end. In these regions the exudate may collect in large amounts, while elsewhere in the cavity there may be scarcely a trace of peritonitis. Not infrequently the exudate may become completely shut off from the cavity by fibrinous adhesions, which, becoming organized, finally form a fibrous connective-tissue capsule enclosing the exudate, which is either absorbed, organized, or undergoes inspissation or calcification. As mentioned above, the omentum plays an important rôle in such encapsulations, which are most often seen in the neighborhood of the appendix and the female pelvic organs. In the case of a perforative peritonitis the exudate may contain, in addition to the purely inflammatory products, also stomach or intestinal contents, bile, urine, etc.

In the more severe cases the entire intestinal wall may be involved, becoming swollen, œdematous, and easily torn. Even in the light cases the subserosa is œdematously swollen and may be easily stripped off from the muscularis. The muscle coats may be completely paralyzed; hence the occurrence of marked tympanites, general or local. On opening the stomach and intestines the mucosa is usually found to be pale, swollen, and œdematous. Likewise the superficial portions of the liver, spleen, gall bladder, etc., are œdematous and swollen, often appearing as if macerated. The gall bladder and the lower edge of the liver in particular may show an extreme œdema. The tissues of the mesentery are swollen, moist, and more easily torn than normally. The mesenteric and retroperitoneal glands are usually pale, soft, and enlarged. Even the muscles of the abdominal wall may be pale and œdematous, and the parietal peritoneum can be easily stripped from its attachments. The omentum is swollen, injected, and œdematous. It is very frequently rolled up into a thick mass, but in the case of surgical or perforative peritonitis it is usually more or less adherent to the site of injury. It may be covered with a thick layer of fibrin and may aid in the encapsulation of the exudate. The diaphragm is usually pushed up to the third or even second rib; the lungs show partial atelectasis, particularly the lower lobes; and the heart is pushed upward and more or less to one side.

Although the changes just described apply to the great majority of cases of peritonitis, yet the limit of variation is great, in so far as the appearances presented by individual cases are concerned. A pure *serous peritonitis* (*peritonitis serosa*) is relatively infrequent. Some fibrin is almost always present, so that the exudate should be more properly termed sero-fibrinous. The fluid exudate is yellowish, slightly cloudy, and contains but few cells, but fibrin flakes are found floating in it. Over the peritoneum there is usually a delicate film of fibrin. A pure *fibrinous peritonitis* is not common as a general process,

but is often seen as a local peritonitis. The serosa is cloudy, dry (*peritonitis sicca*) and covered with sticky fibrin.

When the number of cells in the exudate is so great as to cause a turbidity, the peritonitis may be styled *purulent* (*peritonitis purulenta*). A pure purulent peritonitis is also rare, the character of the exudate being usually that of a *fibrino-purulent* inflammation. The coils are usually fastened together by masses of fibrin, while in the pockets between them a relatively pure purulent exudate is found, usually in large amounts (20–30 litres). The so-called *peritonitis ulcerosa* is a misnomer, the appearances of ulceration over the surfaces of the abdominal organs and the parietal layer of the peritoneum being due to a loss of substance through erosion and pressure. In such cases the purulent exudate may perforate into the stomach, intestine, ureter, bladder, uterus, or through the diaphragm or abdominal wall (*secondary perforative peritonitis*). In the last-named case the perforation is usually located at the navel. This event happens more frequently in children than in adults.

In the case of *putrid peritonitis* the exudate has a foul odor and is irritating to the skin of the operator or prosector. In color it varies from dirty-green to brownish. The fibrin of the exudate and the serosa itself may be likewise dark-colored. Gas may be present in the cavity, and the odor of hydrogen sulphide is often very pronounced even when no perforation has occurred. In the case of a perforation of stomach or intestine food remains or fæces may be found in the exudate. Brownish masses are also sometimes present; on microscopical examination they are found to consist of colonies of bacteria.

An acute *hemorrhagic peritonitis* is rare. It is usually associated with carcinoma or tuberculosis, but occurs also in morbus maculosus Werlhofii and in scurvy. Through the presence of hydrogen sulphide in the exudate the blood pigment may become converted into a hydrogen-sulphide compound, giving a gray or slate color to the exudate and serosa (*pseudomelanosis*). Friedreich has described an especial form of hemorrhagic peritonitis under the name of *hæmatoma peritonei*. In such cases the peritoneal surface is covered with layers of blood clot which are becoming organized, the condition being analogous to the subdural hæmatoma.

Circumscribed peritonitis presents practically the same appearances as the general form, except in being localized through the rapid formation of firm adhesions which prevent the inflammation from spreading (*peritonitis adhæsiva*). These adhesions may quickly become organized. Circumscribed peritonitis occurs most often as a perityphlitis (peri-appendiceal) dependent upon perforation of the appendix, and as a pelvic peritonitis (pelveo-peritonitis) due to diseased conditions of the uterus and its appendages. It may be caused also by perforative processes (ulcer, new growths, etc.) of stomach, intestine, gall bladder, etc., by splenic infarction, hepatic abscess, and other local inflammations of the intraperitoneal organs. The so-called subdiaphragmatic abscess is an encapsulated purulent peritonitis. Similar encysted collections of exudate may be found in any part of the peritoneal cavity, but are more frequent in the regions named. Gonococcic peritonitis is usually circumscribed in the pelvis. The part which the omentum plays in the encapsulation of a local peritonitis has been mentioned above. Through its aid many cases of perforation peritonitis, particularly in the case of the appendix, are restricted to a narrow area. The frequency with which omental adhesions are formed about the appendix, tubes, perforating ulcers, new growths, etc., is evidence of its very great service in limiting peritonitis.

Complications.—The complications of acute peritonitis are many and important. Perforation of the peritoneal exudate into some viscus or through the abdominal walls has been mentioned. Occasionally the pus may break through into two neighboring coils of intestine at the same time, giving rise to the so-called *fistulæ bimucosæ*. Fatal hemorrhage may follow perforation into an abdominal blood-vessel. Metastasis may occur and a general pyæmia may result. It is not uncommon in the case of a severe acute general peritonitis to find at autopsy a beginning pleuritis, pericarditis, or meningitis. Sometimes all the serous membranes may be equally involved (panserositis). Such pathological findings are seen most frequently in puerperal peritonitis.

Microscopical Appearances.—Sections through an acutely inflamed peritoneum present changes which are analogous to those of inflammations of other serous membranes. The surface of the membrane is covered with a more or less thick layer of fibrin containing a varying number of leucocytes. The latter usually show karyorrhexis, the diffusion of the chromatin throughout the fibrin causing the latter to stain bluish. Beneath the exudate the endothelium is degenerated, necrotic, or desquamated. The connective tissue of the basement membrane is œdematous and infiltrated with leucocytes. The lymphatics are greatly dilated and contain fibrin and large numbers of leucocytes. The blood-vessels are also greatly congested and filled with leucocytes. The endothelial cells of both lymph- and blood-vessels are usually somewhat swollen. Scattered hemorrhages of small size may also be found. The subserosa is usually actively involved, the connective tissue being œdematous and infiltrated with leucocytes; the vessels are congested and small hemorrhages may occur. Fibrin threads may be found in the intercellular spaces of both serosa and subserosa. The muscularis is involved to a much less extent. Its vessels are congested and the intermuscular connective tissue is more or less œdematous and contains an increased number of leucocytes. In severe cases the nerve cells of the intestinal wall may present various changes, such as vacuolation, hydropic degeneration, chromatolysis, etc. In the later stages of the inflammation evidences of proliferation are found in the endothelial cells of the blood- and lymph-vessels and in the connective-tissue cells of the serosa and subserosa. Fibroblasts wander out into the fibrin of the exudate and a new formation of capillaries takes place. Even in attacks of peritonitis lasting but five to seven days the organization of the exudate may have advanced considerably. In the further progress of the disease connective-tissue adhesions and false membranes may be formed, or marked thickenings of the peritoneal surfaces may result. Should complete healing take place the newly formed connective tissue becomes scar-like and hyaline, and marked retractions of the omentum and mesentery may be caused. The remains of old organized fibrinous exudates are most frequently seen in the form of tendinous patches or small pearly nodules over the surface of the spleen, liver, or intestine. Extensive thickening of the pelvic peritoneum may result from the healing of circumscribed peritonitis in this region. During the stage of active fibroblastic proliferation such a large mass of granulation tissue may be formed that in the case of a circumscribed peri-appendiceal peritonitis a tumor may be produced which may be mistaken clinically for a malignant neoplasm, and even when examined microscopically might be mistaken for a sarcoma. Such tumor-like masses may also be found in the omentum. Should healing take place the tumor may gradually contract and finally entirely disappear ("disappearing tumor"). The presence of exudate not yet organized, the large number of polymorphonuclear leucocytes showing karyorrhexis, the hypertrophic character of the endothelium of the numerous capillaries, the presence of many plasma cells and phagocytes, the development in areas of a fibrous intercellular substance, etc., are among the points to be considered in making a microscopical diagnosis of tissue removed from such tumor-like formations.

Subacute Peritonitis.—In cases running a slower course the amount of exudate is usually less than in the acute forms, although in some cases in which it is more serous in character the amount may be very large. The adhesions are firmer, organization having progressed to a greater extent. The serosa is thickened, roughened, and wholly lustreless, and is often grayish or slate-colored. The injection of the blood-vessels is much less, and there

is also less œdema of the subserosa. Exacerbations, which are very likely to occur, give the appearances of an acute inflammation. Microscopically the exudate covering the serosa is found to be partly organized, and there is a fibroblastic increase of tissue. The cells of the exudate may show fatty or hydropic degeneration.

Chronic Peritonitis.—Chronic peritonitis may follow an acute process or it may develop insidiously. The changes seen in chronic peritonitis are essentially the same as in the acute process, the chief difference being in the more advanced organization of the exudate with resulting firm adhesions and formation of false membranes, tendinous patches, etc. When numerous adhesions are formed the condition is termed *peritonitis chronica adhæsiva*. The capsule of the liver and spleen may be greatly thickened and hyaline (chronic perihepatitis, chronic perisplenitis). Scar-like thickenings and retractions of the omentum and mesentery may be found (*peritonitis chronica retrahens*), and in the former there may be produced tumor-like masses of granulation tissue. It is usually rolled up above the level of the umbilicus. Marked deformities of the intestine and intraperitoneal organs may be produced by the contraction of the new-formed connective tissue (*peritonitis deformans*). Partial or complete stenosis of the intestine, common duct, ureters, tubes, etc., may result from the contraction or pull of band-like adhesions. Incarceration of portions of the intestinal coils in hernia-like sacs formed by adhesions may also occur. Inasmuch as exacerbations are not infrequently seen in chronic peritonitis the picture of a recent exudation may be added to that of an older process. The *hæmatoma peritonei* of Friedreich mentioned above is associated particularly with a rare form of chronic hemorrhagic peritonitis. Chronic peritonitis may be local or general; the former is the more common. The inflammation may be dry, or a sero-fibrinous exudate may be present; less frequently the exudate is hemorrhagic or purulent.

Local chronic peritonitis is seen most often in the hepatic region (cirrhosis, gall-stones, syphilis, etc.), in the splenic region (perisplenitis), and in the pelvis of the female. In prostitutes a local chronic pelveo-peritonitis is nearly always present in the form of adhesions. The appendix region, the neighborhood of gastric and intestinal ulcers, hernial sacs, etc., are also frequent seats of chronic peritonitis.

Attention has recently been directed to the condition designated "*chronic multiple serositis*" or "*multiple progressive hyaloserositis*" which is characterized by a slowly progressive hyperplasia of the serous membranes with secondary hyaline changes. In the case of the peritoneum the condition is usually most marked over the capsule of the liver or spleen (chronic perihepatitis, chronic perisplenitis). The thickened and hyaline capsule presents an appearance resembling the icing of a cake ("Zuckergussleber" of Curschmann, "iced liver"). An obliterative pericarditis or pleuritis may or may not be coincident with the peritoneal condition. The capsules of the liver and spleen may be involved at the same time or either one may alone show the change, or the condition may be diffuse throughout the entire extent of the peritoneum, or it may occur as a part of a multiple affection of the serous membranes. When affecting chiefly the liver capsule the condition may be the result of a local chronic peritonitis, an acute or subacute hepatitis, chronic mediastinopericarditis, or a chronic obliterative pleuritis. It may also be a part of a Glissonian cirrhosis, perhaps associated with syphilis or tuberculosis. The affection of the splenic capsule is usually the result of a local chronic peritonitis, or is associated with syphilis or tuberculosis. Chronic hyaloserositis is essentially a hyperplastic inflammation, and is probably due to an infection with micro-organisms of a low virulence. In the majority of cases it is probably tuberculous. Microscopically the thickened splenic or hepatic capsule consists of laminated hyaline connective tissue, usually poor in cells, but occasionally containing groups of leucocytes or areas of unorganized fibrin. In some cases, at least, the organization of a fibrinous exudate with subsequent hyaline change of the new connective tissue plays an important, if not the chief, part in the production of the condition.

Peritonitis Carcinomatosa.—Scirrhous carcinoma of the stomach or gall bladder may give rise to secondaries scattered diffusely throughout the peritoneum. The membrane at the same time presents the appearance of a chronic hyaloperitonitis, the entire serosa, intestinal and parietal, as well as the hepatic and splenic capsules, being greatly thickened, dense, and hyaline. Such a condition may very easily be mistaken for a simple chronic peritonitis, inasmuch as appearances suggesting malignancy may not be visible to the naked eye. The diagnosis in some cases can be made only on microscopical examination, since the primary growth may consist only of a dense thickening of the pyloric end of the stomach or of the gall-bladder wall and may not be recognized from the gross appearances. Microscopically the hyaline connective tissue of the thickened peritoneum is seen to contain small nests and cords of epithelial cells, corresponding to those of the carcinomatous infiltration at the primary seat. It is well to bear in mind the fact that the mesenteric and retroperitoneal lymph glands may contain large nests of cancer cells, so that the diagnosis of scirrhous carcinoma may be more easily arrived at by the examination of these glands. The peritoneal condition may therefore be regarded as of the nature of a diffuse carcinomatosis with secondary inflammatory changes. More or less fibrinous exudate may be present over the surface of the thickened membrane, and some free fluid may be present in the cavity.

Experimental Peritonitis.—A number of important experimental studies of peritonitis have been carried out by different observers, particularly with reference to the etiological factors of peritonitis. The part played by various bacteria and by such predisposing factors as chemical irritation, cold, etc., has been studied with the gain of much important knowledge. Other writers have recently studied the character of the cells found in the peritoneal exudate. Beattie has made experimental investigations along this line. After the injection of bacteria into the peritoneal cavity various cells appear in the exudate. Polymorphonuclear leucocytes appear in great numbers on the peritoneal surface, and are found abundantly in from six to fifty-four hours after the injection. In fatal cases they increase up to the time of death of the animal, but in non-fatal cases they diminish in from forty-eight to sixty hours. They act as the chief bacterial phagocytes. Mononuclear phagocytes are also found at all stages, but are most abundant from thirty-six hours onward. They are derived from the endothelium of the serous membrane, of blood-vessels, lymph vessels, lymph spaces, etc. They possess amœboid motion, and are especially phagocytic to other cells, but may also take up bacteria. Great numbers of these cells are always found on the omentum, and Beattie regards them as the most important cells of the peritoneal exudate. The presence of large numbers of these cells, if they give evidences of active function, is a favorable sign. Since the omentum furnishes large numbers of the mononuclear cells in peritonitis this organ must be regarded as an important agent in protecting the body from infection by way of the peritoneum. Both the polymorphonuclear and mononuclear phagocytes are destroyed in the peritoneal sac, the former being largely ingested by the latter. In the case of peritonitis associated with secondary carcinoma of the peritoneum tumor cells may be found in the exudate in addition to the polymorphonuclear and mononuclear phagocytes. As a rule the cancer cells cannot be distinguished from the latter; but if numerous cell-division figures are present, especially atypical forms, it is very likely that such cells come from a new growth.

Symptoms.—*Acute General Peritonitis.*—Peritonitis in the great majority of cases being a secondary disease the symptoms are modified to a greater or less extent by the original trouble. The onset in particular is modified.

Perforative peritonitis may occur suddenly in a person apparently in perfect health. Not infrequently the first intimation of the existence of a gastric or intestinal ulcer is the peritonitis following a perforation. In the case of perforative appendicitis the onset may be equally sudden. On the other hand, the symptoms of perforative peritonitis may be obscured in the case of intestinal tuberculosis, typhoid fever, intestinal obstruction, etc., by the severe local or general symptoms. A circumscribed peritonitis may also become gradually changed into a general condition, the change in symptoms not being so pronounced as to be noted. For example, a localized purulent perityphlitis or a purulent puerperal pelveoperitonitis may become generalized. A pneumococcic peritonitis occurring in association with pneumonia or meningitis may have its onset obscured by the general symptoms.

In spite of these exceptions nearly every case of acute general peritonitis runs a clinical course so typical and characteristic that the recognition of the condition becomes a matter attended by little or no difficulty.

Prodromal symptoms may or may not occur. In the former case they consist of chills, prolonged and repeated chilly sensations, fever, loss of appetite, nausea, vomiting, thirst, diarrhœa or constipation, flatulence, etc.

Pain is the earliest definite symptom, and few cases of acute peritonitis exist without it. In patients who are extremely weak or whose minds are clouded, no complaint of pain may be made, and the condition may in this way escape notice. In nearly every case, however, the pain becomes the most marked and important symptom. It may be local, often referred to the region of the umbilicus, but later usually extends over the entire abdomen. The localization of the pain at the onset of the disease may have some diagnostic value in indicating the possible source of the inflammation, as, for example, in the case of gastric ulcer or a perforating appendicitis. The pain is usually excruciating in character, and may be constant, or it may occur with short remissions followed by exacerbations. Colic-like paroxysms sometimes occur. The abdomen is extremely sensitive, so that even gentle palpation, or even the weight of the bed clothes can hardly be borne. The patient assumes a position which relieves the tension of the abdominal muscles, lying on the back with thighs drawn up and shoulders elevated. Such a position may be maintained for days and weeks as long as the condition lasts. The pain is increased by deep inspirations, voluntary movements, and probably also by intestinal peristalsis. The patient fears particularly such movements as vomiting, coughing, sneezing, defecation and urination, etc. The character of the pain is sometimes described as burning, boring, tearing, lancinating, etc., without much light being thrown upon the conditions causing the especial character. The passage of gas through the coils probably plays an important part in producing the painful attacks. Though in the majority of cases the pain is most severe below the umbilicus, in cases of perforation of the stomach the pain may be referred to the shoulders, back, or chest. In the earlier stages of peritonitis following appendicitis the pain may sometimes be referred to the testicle or the penis. Mackenzie believes that the pain which is caused by pressure over the abdomen is entirely due to muscular and cutaneous hyperæsthesia, the peritoneum itself being devoid of sensory nerves. The board-like hardness of the abdominal muscles in peritonitis he holds to be the result of a violent stimulation passing from the affected organs of the peritoneal cavity to the spinal cord, where the irritation spreads, affecting not only the centres of the sensory nerves, but also those of the muscular nerves. When the patient is at perfect rest the pain may be slight or may even entirely disappear.

The *respiration* is very superficial, rapid, and wholly costal in type. The speech usually becomes an almost imperceptible whisper, occasionally hoarse and high-pitched, resembling the so-called vox cholerica. When the attack is fully established the patient presents a very characteristic appearance, the expression is anxious, the face pinched and the eyes are sunken, the Hippocratic facies being seen in this affection more often than in any other disease except cholera. The severity of the pain is usually expressed by the patient's face; in severe cases the eyes are glassy and staring. Consciousness remains preserved usually until the last; rarely there is delirium, coma, or convulsion at the end.

The abdomen quickly becomes distended, the distention becoming gradually more and more marked, and sometimes reaches such an extent that it seems that the abdominal wall must give way. The skin over the abdomen is smooth, shining, thinned, the superficial veins appearing as blue lines. Fresh lineæ albicantiæ may be seen over the surface. The abdominal muscles are stretched and often of a board-like hardness. The distention is due to the intestinal tympanites, which is sometimes so great that complete paralysis of the intestinal musculature results. The distended coils of intestine can sometimes be traced through the abdominal wall. The more lax the abdominal wall before the beginning of the peritonitis the greater will be the distention; hence the distention is most marked in the puerperal cases. When the abdominal muscles are well developed and the abdominal wall is tense, the convexity may not be great. In some cases the wall may be as hard as a board and flat or even somewhat concave. In the latter case the diagnosis may be very difficult. In the later stages the abdominal distention is increased by the fluid exudate.

Vomiting is an almost constant symptom in peritonitis. It usually begins early in the disease and causes great pain. At first the vomitus consists of food remains, later it consists chiefly of a yellowish bile-stained fluid, and finally becomes greenish. Occasionally the vomitus is brownish-black and possesses a slight fæcal odor. The attacks may be spontaneous or follow the taking of food. In the former case the vomitus consists usually of greenish mucus. Eructations of gas usually accompany the vomiting. The frequency and intensity of the vomiting vary. In some cases nothing can be retained upon the stomach, and the patient's strength is very quickly lost. The cause of the vomiting is not clear; it is probably partly reflex and partly due to pressure upon the stomach. In those cases in which the vomitus has a fæcal character the autopsy usually discloses no intestinal obstruction. It is therefore probable that the condition is due to the paralysis of the intestinal musculature and to the pressure upon the intestine. Toward the close of the attack the vomiting may be replaced by painful *hiccoughs*, which are a source of great torture to the patient. It is probable that this is due to the involvement of the peritoneal surface of the diaphragm. In those cases in which the vomiting is kept up to the end some of the vomitus usually enters the respiratory tract and may give rise to an aspiration pneumonia or gangrene of the lung.

Peritonitis not infrequently begins with *diarrhœa*, which in some cases is associated with tenesmus, or assumes a dysenteric character. The paralysis of the intestinal musculature soon leads to *constipation*, so that this condition becomes an almost constant feature of the disease.

The *tongue* is usually coated, grayish-white or brown; in cases of obstinate vomiting it may be clean and red or fissured. A very disagreeable fœtor is usually present, sometimes almost fæcal in character.

After the chill the body temperature usually rises, reaching 104°–105° F. or higher, but later usually falls. The type of the *fever* is very varied; it may be continuous, intermittent, or remittent. The skin may be cool, while the rectal temperature is high. In the case of collapse the temperature may fall even to subnormal, and the body may be covered with an abundant cold perspiration. Just before death the temperature may rise again and reach a very high point.

The *pulse* is usually very frequent, the increase in rate being out of proportion to the fever, 120–140 per minute not being uncommon. The pulse is at the same time

small and soft, and in very severe cases may become imperceptible.

The number of *respirations* is increased, 30–40 per minute. The increased rate is due partly to the fever, partly to the high position of the diaphragm, and partly to the pain attending abdominal breathing. As mentioned above, the type is costal and the breathing superficial. The cessation of movement of the diaphragm is regarded as a bad sign, some writers considering the prognosis hopeful as long as an inspiratory excursion of the diaphragm can be felt, this being taken as a sign that the peritonitis is not wholly diffuse.

The *subjective* symptoms are chiefly pain, uncontrollable thirst, shortness of breath, and anxiety.

Percussion gives a tympanitic tone over the distended intestine. Dulness over the dependent portions is usually not made out until after considerable exudate has collected. When the tympanites is very marked a large amount of effusion may be present without its being detected on percussion. A change of level of the dulness with change of position does not always take place; the adhesions between the coils preventing the movement of the exudate. Moreover, there is usually too much pain to permit of a careful examination. The liver dulness is diminished, the upper border being pushed upward to the fifth or fourth rib. The splenic dulness cannot usually be made out. The heart is pushed upward, the apex beat dislocated upward and to the left. The movements of the heart in the intercostal spaces are more prominent than normal.

Auscultation of the abdomen does not throw much light upon the condition. Gurgling and splashing sounds may be heard in the intestines. Occasionally friction sounds may be heard, but these are not so common as in pleuritis or pericarditis. In pneumoperitonitis splashing sounds may be produced by shaking the patient. The heart sounds may have a metallic resonance in the case of extreme tympanites. The pulmonary second sound is usually accentuated.

The *urine* is usually diminished in amount, dark, strongly acid, of high specific gravity, and sometimes contains a small amount of albumin. The amount of indican present may be much greater than usual.

Certain writers claim that there is a *local increase of temperature* in the abdominal wall, and that this fact constitutes an important diagnostic factor. The normal temperature of the surface of the abdomen is about 35.5° C.

In the case of *pneumoperitoneum* due to perforation or to formation of gas within the cavity the hepatic dulness is obliterated. The liver dulness may, however, disappear when there is no gas in the cavity; but if the patient is placed upon his left side a clear percussion tone will be heard at the seventh or eighth rib in the right axillary line in the case of pneumoperitoneum. In other cases dulness will be found at this region. The disappearance of the liver dulness anteriorly when pneumoperitoneum does not exist is due to the tilting backward of the organ and the presence between it and the abdominal wall of a loop of distended intestine.

The *course* of an acute general peritonitis is usually very rapid. The most severe cases may terminate fatally within thirty-six to forty-eight hours, while the average case usually lasts five or six days. Since the etiological factors vary so greatly no absolute statements can be made regarding the clinical course. The peritonitis occurring as the result of gastric or intestinal perforation is usually quickly fatal, but much is to be hoped from the surgical treatment of these cases. Puerperal septic peritonitis is likewise usually fatal. Pneumococcic peritonitis is also likely to terminate more or less quickly in the death of the patient. The peritonitis which occurs in connection with arthritis, as well as in all other cases in which the exudate is serous or sero-fibrinous, is much more likely to end in recovery.

In the fatal cases *death* may occur suddenly as if from shock; or in the case of extreme tympanites the high position of the diaphragm may cause death from suffocation. In some cases the final picture is that of a general sepsis or pyæmia. In the great majority of cases the pulse becomes more rapid, the vomiting persists, the bodily powers are quickly exhausted, and the patient dies with symptoms of collapse. In such cases the temperature usually becomes subnormal as the end approaches.

In other cases of less frequent occurrence the disease may drag itself out over weeks and months, assuming the characteristics of a subacute or chronic process. Various complications may occur during such a prolonged course. Rupture of the exudate into the gastro-intestinal tract or through the abdominal wall, etc., is most likely to occur in such cases. In the event of such perforation into the stomach, pus will be found in the vomitus; when into the intestine the pus will appear in the stools; when into the urinary tract the urine will show a sediment of pus; when into the respiratory tract the sputum will be abundant and purulent. In the event of a rupture through the abdominal wall redness, swelling, and œdema will first appear at the affected spot, the skin becomes thinned, fluctuation occurs, and pus finally seeps through small fissures, or an opening of large size may be formed, through which the pus may be forced in streams during coughing, etc. The navel is the most common seat of perforation. In some cases the pus burrows beneath the skin for some distance before it finally breaks through. In other cases some of the exudate may be absorbed or encapsulation may take place. Exacerbations are frequent and death may take place finally from general marasmus. General dropsy, bedsores, albuminuria, etc., characterize the course of such cases.

In the mild cases of general peritonitis following labor, abortion, or menstruation recovery may occur. Even in those cases in which the disease runs a rapid and favorable course disturbances of the digestive tract usually develop, and the patient may die later from intestinal obstruction caused by the contraction of adhesions. A favorable prognosis should not be too hastily given in such cases. Nevertheless, complete recovery may result after a year or longer, even in very severe cases.

Acute Circumscribed Peritonitis.—The local symptoms of this form are similar to those of the general process, but are more limited. The vomiting is not so severe or so persistent as in the general inflammation. Though the general weakness is marked the symptoms of collapse do not occur to the same extent as in general peritonitis. An irregular fever is usually present, running a course suggesting that of a pyæmic affection. The condition is usually very chronic. Many patients die from general debility. Spontaneous evacuation of the encapsulated exudate may take place through perforation into the gastro-intestinal tract, pleura and lungs, abdominal wall, etc. Should the perforation take place into the remaining portion of the peritoneal cavity the peritonitis may become diffuse. According to the location of the inflammation (perisplenitis, perihepatitis, perityphlitis, perimetritis, peripancreatitis, perigastritis, epiploitis, mesenteritis, etc.) various symptoms may arise through the disturbance of function of the affected organ. Pain is usually felt in the affected region. The physical signs are local tumor, dulness, fluctuation, peritoneal friction, etc.

Of the various forms of acute circumscribed peritonitis the condition known as *subphrenic abscess* deserves especial attention. It is due to an encapsulated collection of purulent exudate between the upper surface of the liver, stomach, or spleen, and the diaphragm. Owing to the paralysis of the diaphragm the tumor may rise high into the thorax and may be mistaken for a pleural effusion, especially since a secondary pleuritis is usually present. Hepatic abscess, splenic infarction, splenic abscess, rupture of echinococcus cysts, and gall stones are the more common causes of the condition, but it is not a rare complication of perforating appendicitis.

Perforation Peritonitis.—The peritonitis due to perforation may be local or general. It may run a very

acute course, but when circumscribed is more likely to be chronic. In the case of the sudden perforation, as, for example, of the stomach, intestine, cystic tumor, etc., the patient may feel a sharp tearing sensation, as if something had given way within the body. The severest symptoms of collapse may immediately result. The abdomen may be contracted, hard as a board, and even scaphoid. The slightest touch causes extreme pain. Death may take place within a few hours. In other cases the entrance into the peritoneal cavity of stomach contents, fæces, bile, etc., excites a general peritonitis with symptoms as described above. In the case of perforation of the gastro-intestinal tract gas may also enter the cavity, and the picture of a pneumoperitonitis be presented. The liver and splenic areas of dulness are obliterated unless these organs have become attached to the anterior abdominal wall by means of adhesions. Succussion sounds may be produced, and the respiratory sounds may acquire an amphoric quality.

Puerperal Peritonitis.—This dreaded complication usually appears at from the third to the fifth day after labor. Safety from the condition is usually assumed if the woman reaches the end of the second week without its occurrence. The pain is usually much less intense than in the other forms of general peritonitis, and the tympanites more marked. Chills occur more frequently than in other forms and diarrhœa is almost always present, the discharges often becoming bloody and of the character of a dysentery. The vomiting is especially obstinate. The lochial discharges often become offensive. The peritoneal exudate is usually more abundant and more purulent in character than in other forms, and not infrequently becomes putrid. The mortality is great, death taking place with symptoms of general sepsis usually between the fifth and twelfth days.

Infantile Peritonitis.—*Fœtal* peritonitis occurs between the seventh and ninth months of intra-uterine life. Syphilis is the chief etiological factor. Infection of the umbilicus may lead to a *peritonitis neonatorum*. The children of mothers suffering from puerperal sepsis are especially likely to become infected. In addition to the local symptoms of distention, pain, etc., there is usually a picture of general sepsis or pyæmia. The condition is almost always fatal. A peritonitis may also develop in infants and young children (*peritonitis infantium*) as the result of syphilis, or of infection with pyogenic organisms, the pneumococcus, gonococcus, etc. In the great majority of cases peritonitis in young children is the result of appendicitis. In peritonitis which occurs in young girls the possibility of a gonococcic infection should always be borne in mind and the genital passages examined for the existence of such disease. Non-gonococcal vulvo-vaginitis rarely spreads to the peritoneum. Pneumococcic peritonitis is more common in girl than in boy infants. The infection is probably through the genital tract. The onset is usually very sudden, with abdominal pain, fever, and vomiting. The course of the affection is very similar to that of pneumonia, the active symptoms subsiding in from seven to ten days, but the abdomen remains distended, and later the presence of an exudate becomes manifest. The prognosis in the cases of general infection is not good, but when the inflammation is localized in the pelvis it is more favorable.

Chronic Peritonitis.—In the majority of cases chronic diffuse peritonitis is the sequela of an acute inflammation, although such an occurrence is relatively rare. Usually no sharp line can be drawn between the two; the symptoms of an intense acute process gradually abate and are replaced by those of a chronic type. In some cases the chronic inflammation develops as the sequela of a number of acute attacks; in others the onset is slow and insidious. The pain, abdominal tenderness, and distention are never so marked as in the acute cases. The distention is usually moderate and often asymmetrical, certain coils of intestine being especially prominent. Sometimes the abdomen is flat or even scaphoid, the walls are hard and board-like. On palpation the thickening of the omentum and mesentery, as well as the fibrous adhesions between the coils, may be made out as tumor-like masses or as uneven prominences. When an effusion is present palpation may be negative. A friction rub may occasionally be felt. In some cases the abdomen may be so tense that nothing can be felt through it. Cases of chronic peritonitis, not due to tuberculosis or complicated with other conditions, do not usually show much exudation. The course is very protracted. Recovery may follow the absorption and organization of the exudate, or its escape by perforation from the cavity. Death usually results from general marasmus. The healing of the inflammation may be followed later by stenosis and intestinal obstruction, which may result fatally. Occlusions of the common duct by the contraction of adhesions may cause a chronic obstructive jaundice.

A peculiar form of chronic serous peritonitis occurs in children, appearing under the form of a chronic ascites. It occurs most frequently between the ages of two and ten, and in girls at the age of puberty. The abdomen is distended by the exudate, which is usually quite abundant, serous in character, and freely movable. The affected children are anæmic, more or less weak, but do not lose much in weight and do not suffer pain. The lower extremities may become œdematous. The exudate may apparently entirely disappear and then return. The course may last many months and may terminate in complete recovery. The exact nature of the affection is unknown. Trauma, inflammation of the gastro-intestinal tract, lymph glands, and genital tract, etc., have been adduced as etiological factors. It is possible that the condition represents an infection of the peritoneum with tubercle bacilli of low virulence. In the fatal cases death results from an increasing marasmus.

Tuberculosis of the Peritoneum.—Tuberculous disease of the peritoneum is of especial interest because of its peculiar clinical course and the fact that the condition may undergo spontaneous healing after laparotomy. A distinction is drawn by some writers between pure tuberculosis of the peritoneum and a tuberculous peritonitis; but such a distinction, while based upon pathological grounds, has but little practical value, the first condition rarely presenting clinical signs.

Simple tuberculosis of the peritoneum without accompanying inflammation or exudation is usually secondary to an acute miliary or chronic pulmonary tuberculosis. It may be secondary also to tuberculosis of the bronchial or subperitoneal lymph glands, genito-urinary tuberculosis, tuberculosis of the pleura, adrenal bodies, etc. In the great majority of cases the infection of the peritoneum proceeds from tuberculous ulcers of the intestine or caseating mesenteric glands. In rare cases it may be primary. Small grayish tubercles are found scattered over the peritoneum. On microscopical examination they consist of epithelioid cells and numerous giant cells containing tubercle bacilli. Caseating centres may be seen in the larger ones; but inflammatory changes in the neighboring peritoneum are usually wanting. The tubercles are almost always more numerous in the omentum. When very small the tubercles may not be recognized at operation or autopsy; the larger ones are recognized by their grayish color and yellowish centres. Though often very numerous the tubercles are usually circumscribed. There are no symptoms, the condition usually being discovered at autopsy, or in the event of a laparotomy.

Tuberculous peritonitis—tuberculosis with inflammation and exudation—exists in a great variety of forms which have been variously classified by different authors. The most common forms are: *acute miliary tuberculosis* with sero-fibrinous or sero-hemorrhagic exudation; *chronic tuberculous ascites* with small tubercles which show little caseation; *chronic fibro-caseous tuberculous peritonitis* with purulent or fibrino-purulent exudate; *chronic hyperplastic tuberculous peritonitis*; *chronic fibroid tuberculosis* with little or no exudation, the serous surfaces being fastened together by adhesions.

The appearances at autopsy or operation may vary

greatly. In the majority of cases two types predominate: the *adhesive* form and that with *free fluid exudate*. The former is the more common. The coils and the abdominal organs are matted together and to the parietal peritoneum by numerous firm adhesions, in which there are found numerous tubercles or caseous masses. The spaces between the adhesions are filled with a purulent, fibrino-purulent, or hemorrhagic exudate, or, if perforation into the bowel has occurred, with exudate containing fæcal material. Such perforation is not uncommon and fæcal fistulæ may be formed. The adhesions between the liver and spleen and the diaphragm are usually very firm. The omentum is thickened and rolled up, and its boundaries are lost in the general adhesions. In many cases it is almost impossible to orient the abdominal organs, everything being so densely bound together by adhesions, all free surfaces being covered with a thick yellowish or grayish layer of fibrino-purulent exudate. In the second type the peritoneal surface is covered or strewn with numerous tubercles which are more or less confluent. Caseation is usually advanced to a greater or less extent. In the later stages the entire peritoneum becomes covered with a layer of tuberculous granulation tissue containing caseous centres. Adhesions are not numerous and the peritoneal cavity contains a large amount of serous or sero-fibrinous exudate.

In the chronic fibroid form the peritoneum is thickened and hyaline; adhesions are numerous, but there is little or no fluid exudate. The surface of the thickened peritoneum is usually covered with a fibrinous layer. Circumscribed tubercles may be entirely absent, likewise caseation. The spleen and liver may be covered with a thick hyaline layer, the appearances in general resembling those of hyaloserositis, as mentioned above, or the condition may be mistaken for scirrhous carcinoma. On microscopical examination tubercles are found embedded in the masses of fibroid tissue. These usually contain but few bacilli. In the chronic fibro-caseous form large caseating masses may be found in the adhesions or in the peritoneal surface. The chronic hyperplastic form is characterized by the formation of tumor-like masses of tuberculous granulation tissue. The mesentery may become enormously thickened, and the condition may be mistaken for a new growth. A hyperplastic tuberculosis of the intestinal wall is usually found in association with such cases. Such tumor-like masses are encountered most frequently in the right iliac region. Tuberculous tumor-like masses may also be found in the omentum.

Tuberculous peritonitis occurs at all ages, but is most common in middle adult life. The majority of cases appear to occur in females, although many statistics show a majority of males affected. Children are not infrequently affected. According to Osler the condition, in America, is more frequently found in negroes than in the white race. In the female, tuberculous peritonitis is more frequently associated with tuberculosis of the tubes; in children the infection usually comes from the intestines. The condition not infrequently occurs as a terminal infection in hepatic cirrhosis.

The symptoms of tuberculous peritonitis vary greatly. The condition may be entirely latent, and discovered only by accident. In other cases the symptoms may be so severe as to suggest intestinal obstruction. In many instances the onset is like that of an acute general peritonitis. Other cases still resemble typhoid fever and may be mistaken for this disease. The clinical picture varies to such an extent that no very general description can be given. Ascites is usually present, though the amount of exudate may be small. In the acute cases the abdomen may be distended by tympanites, and meteorism is also of frequent occurrence in the late stages of the adhesive form. Fever is always present, though sometimes light. It may be remittent, intermittent, or continuous, and may reach 103°–104° F. A subnormal temperature is not uncommon in the chronic cases, the temperature for days in some cases running 95°–97° F. The patient may appear well nourished or may be emaciated and cachectic. Gastro-intestinal disturbances are the rule, and the bowels are either constipated or loose. The skin sometimes shows pigmentation, and the condition may be mistaken for Addison's disease. The two conditions may, however, exist together. In those cases in which the tuberculous peritonitis is secondary to chronic tuberculosis elsewhere the symptoms of the former may be overshadowed by those of the primary affection. An important local sign in tuberculous peritonitis is the presence of tumor-like masses in the abdomen. These may be due to omental thickening, encapsulated exudation, thickening of the intestinal coils, enlargement of the mesenteric glands, caseating masses, nodules of tuberculous granulation tissue, etc. A friction rub may often be felt over the tumors. The omentum is frequently rolled up and thickened, forming a rope-like tumor lying transversely across the abdomen above the level of the umbilicus. In connection with the symptoms this local sign is of great importance in the diagnosis of tuberculous peritonitis.

The disease pursues a varied course. Spontaneous healing may occur. In the severe acute cases death may take place suddenly as in acute general peritonitis not due to tuberculosis. In the chronic cases the patient may gradually become marasmic and die from general weakness. The course of the affection is subject to various complications which may bring about a fatal termination. Obstruction of the intestine from the contraction of adhesions, perforation of the exudate into neighboring organs, fatal hemorrhage, etc., are the most common of these. Death may take place from the primary tuberculosis, or a general miliary tuberculosis may terminate the case. The prognosis in tuberculous peritonitis has, however, been greatly modified by the results of laparotomy.

Diagnosis.—The diagnosis of acute general peritonitis is usually very easy in those cases in which there is a characteristic picture of abdominal tenderness and distention, vomiting, and collapse. The starting-point of the inflammation is often very evident in cases in which a primary condition, such as typhoid fever, gastric ulcer, puerperal infection, etc., has already been recognized. Careful inquiry and search for such a cause should always be made. A history of previous attacks suggesting appendicitis, of pelvic disease, gastric ulcer, etc., aids greatly in establishing the starting-point. Such a cause cannot always be easily determined. Since many cases are first seen only after the tenderness and distention are marked, the physical examination cannot always be as thoroughly carried out as is desirable. In such cases the pelvic organs should be examined thoroughly. In some cases the diagnosis becomes very difficult, since similar symptoms may be produced by other conditions. Acute enterocolitis, acute intestinal obstruction, intestinal ulcers, acute hemorrhagic pancreatitis, ruptured tubal gestation, embolism of the superior mesenteric artery, rupture of an abdominal aneurism, etc., may present the picture of peritonitis so that it may be impossible to say whether the latter condition has been set up or not. A diagnosis of peritonitis may be given under these conditions when no evidences of it can be found at autopsy. The mistake may be easily made in those cases of typhoid fever in which the tympanites, abdominal pain, and constitutional symptoms are very marked. The presence of parasites in the intestinal tract may also give rise to symptoms suggesting peritonitis. In those cases in which the local symptoms are not marked, while the general collapse is severe, the diagnosis may be entirely missed.

The diagnosis of circumscribed peritonitis is almost wholly dependent upon the recognition of the condition from which the inflammation proceeds. This cannot always be accomplished, and it is often necessary to study the case for some time before a diagnosis can be made. The condition is most often mistaken for a tumor. On the other hand, the distended bladder and pregnant uterus have been mistaken for peritonitis. In doubtful cases aspiration of local tumors should always be carried out.

The diagnosis of chronic peritonitis is sometimes very difficult in so far as a differentiation between simple chronic peritonitis and tuberculous peritonitis is concerned. It may be borne in mind, however, that the former condition is very rare. In those cases in which it is a sequela of an acute process the previous history of the case usually clears up the matter, but in those cases in which the disease develops gradually and insidiously the determination of the nature of the process may be very difficult. The patient's family and individual history must be considered, a careful examination of the thorax and genitals must be made, the abdomen aspirated, and the exudate examined. A hemorrhagic exudate favors tuberculosis. Carcinoma may be diagnosed by the finding in the exudate of small bits of tumor tissue or cells containing atypical division figures. The exudate should also be stained for tubercle bacilli, and animal inoculations may be made. The tuberculin test may also be given. The occurrence of pulmonary, pleuritic, or genito-urinary tuberculosis makes it almost certain that the peritoneal condition is likewise tuberculous. In children the symptoms of the condition known as *tabes mesenterica* are chiefly due to the tuberculous peritonitis present. Tuberculous peritonitis is often a terminal event in hepatic cirrhosis.

Blood Examination.—The red cells are usually diminished in all forms of peritonitis, to a slight or moderate degree in acute forms, but in the chronic cases the anæmia may be marked. During the acute febrile stage the leucocytes are usually slightly increased. In purulent peritonitis the leucocytosis may be more marked, but sometimes is not present or the leucocytes may even be diminished. In perforative peritonitis the beginning of the inflammation may be marked by a leucocytosis. In typhoid fever perforation may be marked by an increase of the polymorphonuclear leucocytes, or the percentage of these may rise without an increase in the total number, or the leucocytes may not be affected. Likewise in appendicitis a very high leucocytosis is suggestive of a beginning peritonitis. In tuberculous peritonitis without obstruction and secondary infection with pyogenic organisms, the leucocyte count is usually low. As a rule leucocytosis in this disease is a sign of a complication.

Hysterical Peritonitis.—Cases have been reported of hysterical conditions in which all the symptoms of peritonitis were simulated: sudden onset, abdominal distention, pain and tenderness, vomiting, symptoms of collapse, etc. Fever may also be present. The cases usually give a history of recurrent attacks without apparent cause. Other hysterical symptoms may be wanting so that a mistaken diagnosis may easily be made.

Treatment.—The treatment of acute peritonitis has been much discussed in recent years, particularly from the operative side, and as a result of improved surgical methods the prognosis in this so frequently fatal condition has been greatly improved. There is much conflicting opinion as to the exact details of the treatment, and various writers even disagree as to more essential points. A survey of the literature, however, seems to indicate that the principle of early surgical interference is gaining ground. As a prophylactic measure in the case of an impending perforation operation has in some quarters met with notable success. With improvement of the surgical technique much may be hoped from the early surgical treatment of cases of acute general peritonitis, and it is not improbable that this disease, at present so dreaded, may be divested of much of its importance.

The older treatment may be summed up as follows: rest, opium or morphine, local applications, hot or cold, local application of leeches, milk diet, ice, small quantities of soda water, etc. In cases of distention the intestines were sometimes tapped with a fine trocar. The intestinal tube was also used to remove gas from the large bowel. Much discussion has also been waged over the use of salines in this condition, some authorities advocating them as an aid to the removal of the exudate, others condemning such use on the ground of danger in the case of intestinal lesions.

While in general the above outline of treatment is still carried out in many cases, important modifications have been made, and the surgical treatment is coming more and more to the foreground. Mikulicz, Krönlein, Oberst, Wagner, Trever, Péan, and Körte were among the first to advise laparotomy for general peritonitis. Many other writers have recently followed in their lead. The operative treatment in general consists of opening the abdomen, removing the exudate as completely as possible, the so-called "toilet of the peritoneum," and after-drainage. The earlier in the disease, especially in the case of perforative peritonitis, the more likely is the operation to be successful. Authorities differ in their views as to the value of washing out the peritoneal cavity. Some recommend very highly the use of large quantities of sterile physiological salt solution, all parts of the abdomen being thoroughly flushed. This seems a rational proceeding, and from the published reports a number of cases have undoubtedly been saved by it. Appropriate general treatment is of course given, intravenous saline injections being freely used during the after-treatment. In those cases in which adhesions have already formed the washing out of the exudate is more difficult and less perfect. This fact is therefore the chief reason for operating as early in the disease as possible. Mikulicz advises several incisions for the purpose of draining and flushing localized collections of exudate.

On the other hand, Krogius does not advise the flushing out of the cavity, apparently for the reason that he does not think it accomplishes the desired purpose. He recommends the dry absorption of the exudate, all parts of the peritoneal surface being thoroughly mopped with sterile gauze compresses and particular attention being paid to the pelvis and the subphrenic space. In order to render all parts of the peritoneum accessible he makes two incisions through the abdominal wall, one along the lateral border of the right rectus, the other along the lateral border of the left. If the exudate in the pelvis cannot be removed through these openings, he advises a counter-opening in the posterior wall of the fornix vaginæ in women, and a parasacral opening in males. After cleansing the peritoneum as perfectly as possible, large Mikulicz iodoform tampons are placed in the pelvis and in the upper and lower portions of the abdominal cavity. These become offensive in a few days and are renewed, the outer dressings being frequently changed. In addition he uses intravenous saline injections, intestinal irrigation, and morphine when necessary. The occurrence of secondary collections of exudate, particularly subphrenic abscess, should be watched for and when found they should be opened and cleansed. Although these principles are applied chiefly to perforative peritonitis occurring in appendicitis they may be utilized in the treatment of all forms of acute general peritonitis.

The surgical treatment is particularly applicable to local circumscribed peritonitis. The encapsulated exudate should be evacuated by incision or puncture, and the cavity washed and treated as a chronic abscess cavity. The details concerning drainage, packing, after-treatment, etc., must be left to the judgment of the operator.

In the case of subphrenic abscess an incision may be made at the edge of the ribs, or the transpleural route may be followed by resecting several ribs. In the chronic forms with multiple adhesions relatively little can be expected from operative procedures.

In the case of tuberculous peritonitis laparotomy is at present the only method of treatment offering hope of improvement or cure, and is universally advised for this condition. The fact that a tuberculous peritonitis may spontaneously heal after laparotomy was accidentally discovered by Spencer Wells in 1862. So much has been written upon this subject that the reader is referred to some one of the recent monographs relating to it. The relation between the laparotomy and the cure of the tuberculosis is wholly unknown, although numerous theories—effects of daylight, evaporation, irritation of

the peritoneal surface, promotion of healthy granulation-tissue formation, increase of the peritoneal resistance, hyperleucocytosis, increased bactericidal action of the exudate, etc.—have been advanced in explanation. Surgeons differ very much in the details of technique in their operations upon such cases. Some open the abdomen and remove the exudate with dry sponges; others flush with warm physiological salt solution; others still wash out the cavity with solutions of salicylic acid, etc. There is also a difference of method in regard to the removal of the organs (tubes, lymph glands, etc.) primarily affected. In general it may be stated that laparotomy is indicated in all cases of tuberculous peritonitis in which the general condition of the patient permits, or in which there is no evidence of cerebral, pulmonary, or extensive glandular or bone tuberculosis. The medicinal treatment of tuberculous peritonitis is advised in some cases, the administration of iodoform as well as its use by inunction having been reported as resulting in cures. Cases of cure have also been reported as following the use of tuberculin.

Very recently a number of writers have been advising conservatism in the treatment of acute general peritonitis by operation. Those who advocate a medicinal method modify the older methods by giving no food by the mouth, employing rectal feeding, allowing no ice, checking thirst by wet gauze to lips and by rectal injections, giving no cathartics, administering small doses of morphine, and applying continued cold to the abdomen. This treatment is based upon the theory that the peritoneal exudate itself may weaken the virulence of or destroy the germs gaining entrance to the cavity. Alcohol has been strongly advised in the treatment of puerperal peritonitis, large and frequent doses being given.

The injection of purgatives directly into the intestinal canal has been advised and as strongly condemned.

Some surgeons advise against operation in sthenic cases of perforative peritonitis without symptoms of sepsis, on the ground that spontaneous resolution may occur. There is, however, a great danger that such cases may under the influence of morphine be allowed to drift along until too late.

Hot vaginal douches have been strongly recommended in cases of pelvic peritonitis. If the external genitals are protected injections of water at 40° C. may be given without discomfort. The pelvis should be elevated, and about 4–5 litres of water used for the irrigation daily. Tampons of glycerin or potassium iodide with glycerin are applied after the irrigation. Stratz in particular claims good results from the application of this method in pelvic peritonitis associated with pyosalpinx.

The statistics of the results of the treatment of acute general peritonitis by operation are very encouraging. Krogius in his monograph published in 1901 has made an elaborate study of the results of operation in general peritonitis following appendicitis. The percentage of cures ranged from 28.5 to 46.

Surgical interference in the case of impending perforation of gastric or intestinal ulcers, appendicitis, rupture of sac in ectopic gestation, salpingitis, necrotic ovarian cystomata or subserous uterine fibromata, hemorrhagic pancreatitis, etc., has proved of the very greatest value as a prophylactic measure. With improved methods of diagnosis much may be hoped for by the further development of such prophylactic operations.

The literature of peritonitis is enormous. Collections of bibliography will be found in the article by Döderlein in Veit's "Handbuch der Gynäkologie," and in the one by Eichhorst in Eulenburg's "Real-Encyclopädie." An exhaustive review of the literature of peritonitis from the year 1885 to 1900 is given by von Bruns (*Cent. f. allg. path. u. anat.* 1901). *Alfred Scott Warthin.*

PHYSICIAN, RELATION OF, TO THE LAW.—In this we have a subject of much interest and importance, yet one that is too little known among the profession at large. Experience, while a valuable teacher, is, where the law is concerned, a very expensive one; so it is the duty of every practitioner to familiarize himself with the laws having a medical aspect, remembering that local, not national, statutes prevail.

In several States medical jurisprudence is one of the subjects of examination as conducted by the State Board of Examination and Registration, and is given equal importance with the other branches, as it should be, for there is no more pitiful sight than to see a medical witness, bright in other subjects, held up to ridicule by attorneys because of ignorance of the legal requirements of the particular case in question.

Judges throughout the Union try to sustain the same rulings along general lines, but it is impossible to lay down fixed rules for all sections of the country in an article of this nature, as the wording of the statutes differs in almost every State; hence they are capable of various interpretations.

License to Practise.—In many of the States good laws have been enacted requiring that the applicant for license present a diploma from a recognized school, showing the necessary training to qualify him for the work which he desires to undertake. Some States, in addition to the presentation of a diploma, require an examination before a State or local board, and will admit no one to the practice of medicine and surgery until a certificate of qualification is issued to the applicant by the Board of Examiners.

After the applicant has received the necessary State documents it is his duty to present the same and his diploma for record to the clerk of the county in which he desires to locate. In case of removal from one county to another the papers must be again recorded in the office of the county clerk. The law must be complied with in every particular, else non-recognition will result if he should be called into court.

If one is located near a county or State line, cases can be attended in the adjoining county or State without a record in the same, provided the practitioner be legally recognized in the county and State in which he is located.

In case of change of location to another State all the local laws must be investigated and fully complied with, the physician going before examining boards if necessary.

As a measure cannot be made retroactive, those who have qualified under former acts are entitled to all the rights and benefits of the law existing at the time of their qualification. In many of our Western and Southern States are to be found legal practitioners who received their medical training as members of a hospital corps during the civil war, or as apprentices of physicians who established themselves in a legal way under the very lax laws that formerly covered the practice of medicine in these localities. Many of these men, being keen observers, and having had the advantages of short post-graduate courses, do much good.

Different Schools.—Under the law the members of the different schools have equal rights. Each is allowed to practise the method in which he has been trained, and he can recover by law such fees as he can prove that he has earned, even if men of other schools testify that the treatment given was not all that it should have been. Decisions have been rendered in several States granting freedom of practice to osteopaths when it was fully demonstrated that their principles in the handling of infectious and malignant cases were faulty.

Malpractice.—In order to recover in a malpractice suit it is necessary to prove that the attending physician or surgeon did not use or display ordinary skill in handling the case in question. This ruling gives a wide latitude in arriving at what constitutes "ordinary skill." A city practitioner, with vast opportunities in hospital work, is expected to have greater skill than the man in country practice whose opportunities are necessarily limited.

A recent ruling of the Superior Court of Cincinnati set aside a judgment rendered in favor of the plaintiff by a lower court, on the ground that expert testimony had not been introduced to show that the attending physician had failed to use or display ordinary skill and care in the

handling of this particular case. This ruling is most wise and will no doubt be the cause of much less annoyance, to say nothing of loss of time and money, to the profession generally, as unscrupulous attorneys have in recent years been filing suits against physicians who were fortunate enough to possess funds or property, in the hope of blackmailing by a so-called compromise, realizing that the majority of men would rather pay them a fee than stand suit under the older rulings.

Like others under the law the physician is liable for damages if he is careless and neglectful in his work. When he is employed to treat a case the contract is implied, and the person or persons employing the medical man are to understand, when the case is accepted, that ordinary skill is to be shown.

Suggestive Therapeutics.—This subject, which has attracted considerable attention in recent years, is one that has its legal complications if carried too far.

A Cincinnati physician was recently indicted on the charge of obtaining money under false pretense as a result of erroneous ideas as to the scope of this line of treatment. A woman who had been under the care of a number of physicians for some time, going first to one and then to another, decided to make another change and called in the man in question. After going into her history, perhaps realizing that his predecessors had done all that was possible in a strictly medical way, he decided that hers was a good case for suggestion, and to this end informed her that she had a tumor which it would be necessary for him to remove. The patient consented and was removed to a hospital for the operation. As an endometritis existed, the womb was curetted, and, after the effects of the anæsthetic had disappeared, the patient was informed that the operation was successful. The attending physician reported that the recovery was rapid, and that the patient had fully recovered from all pre-existing symptoms. After a time the patient asked to be shown the tumor which had been removed. Several excuses were offered, but the patient was persistent; so, to continue the suggestion, the woman was shown a piece of beef so arranged as to resemble a tumor. In some manner it was suggested that a section be made and studied by a pathologist to ascertain the nature of the growth. This suggestion was acted upon and the "tumor" was sent to a well-known man for examination and report, with the result that criminal proceedings were begun against the too ardent advocate of suggestion.

In all cases in which suggestion is likely to benefit, members of the family should be consulted and their consent and co-operation obtained. If actual deception is considered necessary a consultation should be arranged, all the facts bearing on the case reduced to writing, and the document signed by the attending physician, the consultant, and some responsible member of the family, and then carefully filed for reference.

In all cases of suggestion the charges made for service rendered must be in accordance with the work actually performed, else fraud will be claimed and established.

Cases Having a Legal Aspect.—All cases of this nature should be considered in every possible detail, and full notes should immediately be made and recorded in a permanent form for future references. A judge is always of the opinion that a doctor should notice everything, and if he fails in his examination on the witness stand, the public is ready to censure him and the opposing attorneys make light of his ability in their arguments.

If a physician is called to see an individual dying as the result of accident, assault, or attempt at self-destruction, who is capable of making an ante-mortem statement, he should insist that the latter be reduced to writing, signed and witnessed. Before his statement is taken the patient must be informed that death is certain to follow, as dying declarations are of great legal importance, and this point must always be made. The simple statement of an injured person who may be of the opinion that recovery will follow, is of very little value.

When viewing a dead body the physician should note its position, not alone as regards the relation of its members and the surface on which it lies, but also as regards its relation to all surrounding objects. Very careful inspection must be made of the surface of the body and of all wounds, scars, marks, livid spots, and other abnormal conditions; they should be measured and the results should be recorded, together with exact descriptions and a statement of their anatomical relations.

As rigor mortis is of value in determining the state of health at the time of death, this feature must not be overlooked. A note must also be made in regard to the following: Whether the surface of the body is livid or pallid, what expression the face bears; whether the body is warm or cold, as revealed by the temperature of the mouth or the axilla; the exact time at which the body was seen; the condition and nature of the clothing; the contents of the pockets; whether there was any jewelry; at what time—giving hour and place—the person was last seen alive, and whether he or she was alone; if vomited matter is present, collect some of it for chemical analysis; note the presence or absence of weapons, drugs, bottles, or other possible clews.

If a post-mortem examination is necessary to establish the cause of death, every vital organ should be thoroughly examined. The stomach and intestines should be examined for inflammation, and if such areas are found the exact seat and possible nature must be determined. The contents should be collected for examination. The amount, odor, color, and other characteristics are to be noted. If death by poisoning is suspected, the stomach, liver, intestines, and kidneys should be removed for a chemical examination. All vessels used for the collection of vomit, or of other fluids and organs removed, must be known to be perfectly clean and not to have been where contamination with arsenic, strychnine, or mercury could have been possible. Note whether the rectum is empty or filled with fæces; the latter condition indicating that purging could not have taken place. Carefully examine the lips, mouth, pharynx, larynx, œsophagus, and trachea for evidences of the corrosive action of poison.

Note whether there is an abnormal amount of fluid in the pleural cavity, pericardium, cranium, or spinal canal. Thoroughly investigate the action of the valves of the heart.

In cases in which death has resulted from the slow action of poison it is important to investigate the changes which may have taken place in the kidneys and liver. In all cases of death from an unknown cause the best way of arriving at a definite conclusion as to whether death was due to natural or to violent means is by the slow process of exclusion. Full notes along this line will make the position of the medical witness secure, as he is then prepared to meet the attack of attorneys when by cross-examination they try to make the point that death could have resulted from other causes.

When the medical man is called upon to make an examination of a body that has been buried, it is necessary that the body be identified by some one who can positively state that the body in question is the one ordered examined, else the point will be made and sustained that it is possible that the wrong body was exhumed.

Criminal Assault.—This is a subject often brought to the attention of the medical witness, especially in the case of children below the age of ten. Noma pudendi, when discovered by those in charge, is often thought to be the result of an assault, and the afflicted child, not understanding the true nature of the questions asked, will make admissions that result in serious charges being preferred against an innocent person. The other extreme is to be considered at all times in connection with assault, as in rare cases only the most careful examination will reveal physical signs; for wounds and abrasions of the hymen and vagina heal rapidly.

Casper[1] reports a case in which, on examination eleven days after the assault, no signs of the outrage could be observed.

The leucorrhœa common in childhood is often the cause of rape charges. Children of a scrofulous habit

may present points of ulceration about the vagina and vulva, accompanied by a purulent vaginal discharge, so that in any case the presence or absence of gonococci must first be determined and deductions made accordingly.

A child, as a rule, makes little or no resistance at the time of assault; so the bruises and other marks of violence usually observed in older females are absent and the case resolves itself into ascertaining the cause of abnormal conditions about the genital tract.

As false charges are sometimes preferred by older females, it should always be the rule to look upon all cases from this point of view when beginning the examination. If marks of violence are shown, ascertain the time of the alleged assault, and observe whether the wounds or bruises are older than the time indicated; also obtain all the facts as to the manner of the assault, and note whether the marks of violence presented could have resulted in the manner described.

When an examination of the genital tract is made it must be remembered that the hymen is at times destroyed as the result of a purulent discharge, and also that, in some women, it is destroyed at the beginning of the menstrual period. On the other hand, the presence of an intact hymen is not a positive sign that penetration has not taken place. The important thing, in such cases, is to determine whether or not the vaginal canal has been dilated.

In the event of assault on a married woman, or on one who is not a virgin, evidences of injury to the genital tract may or may not exist. If the assailant is alone in his deed, marks of violence are always to be found about the person of the victim, often including the vulva and vagina, for the resistance offered causes undue force to be used in penetrating. If the assailant, however, has assistance, either manual or in the form of drugs, no signs of assault may be present. Where drugs have been administered, their character must be discovered, if possible, and their physiological action fully investigated, in order that it may be shown that hallucinations have not led to the making of the charge. The hallucinations produced by the administration of anæsthetics for slight operations have resulted in dentists being accused of rape.

A case of extreme interest is that of a young woman who was violated while asleep. She had returned from a long walk with her accepted admirer, had drunk a glass of ale, then had fallen asleep in his presence, and the assault followed. Owing to the fact that she was an unusually heavy sleeper, the pain produced by laceration of the hymen and distention of the parts had not been sufficient to awaken her. An examination by a competent medical man revealed the usual physical signs of recent defloration, and the assailant admitted his guilt when charged with the crime.

The medical witness is usually concerned in cases of young children and the feeble-minded; the testimony of the victim commonly establishing the charge in adult cases.

Criminal Abortion.—While we, as a rule, divide the expulsion of the fœtus before the normal termination of intra-uterine life into abortion, miscarriage, and premature delivery, the law regards all under the one head.

It is the duty of the medical witness to distinguish between natural and violent abortion, and, if the cause be violence, to ascertain whether it was criminal or accidental in character. Criminal abortion may be produced by mechanical means or by the use of drugs acting upon the uterus. When mechanical means are used, marks of the violence can usually be demonstrated on the mother and on the expelled fœtus, unless the work has been done by one thoroughly familiar with the anatomy of the parts, and who exercises great care when he introduces the instrument for the purpose of rupturing the membranes.

The use of medicinal substances, by profoundly shocking the system and in this indirect way affecting the uterus, at times produces abortion. When seen the patient is usually giddy, nauseated, and purging. Drugs, even ergot, can be expected to cause an evacuation of the uterus only after the third month of gestation, the muscle fibres not being well enough developed prior to this time to respond; in fact, it is rare that the effect can be obtained until the fifth month of pregnancy is reached.

The diagnosis, shortly after evacuation, is rendered easy by a careful examination, which should always be made, as cases of feigned abortion are on record and similar ones will no doubt occur again.

When a physician is called to see a case in which the evacuation of the uterus seems imperative, he should request a consultation, and a full and complete history should be obtained and reduced to writing, if abortion is decided upon.

Infanticide.—By this term we mean the murder of a new-born child. In perhaps no class of cases is the medical expert so handicapped as in this. Many children die shortly after birth, yet live long enough for well-known evidences of this fact to exist, and the question to be determined is whether death was due to natural causes or to violence. Marks of injury may show on almost any part of the body of the infant and be due to forces acting at the time of delivery. The first question that presents itself when one views a dead infant, is what is its age; and in this connection it must be remembered that the younger in uterine age the infant is, the greater the danger of death at birth or shortly after.

The child should be weighed and measured and all details in regard to its degree of development should be recorded, especial care being taken to note the size of the head as compared with that of the trunk, the degree of ossification, the color and thickness of the skin, and whether the surface of the brain is smooth or already presents convolutions. If the child is fully developed it must be determined whether it lived to breathe and whether it was born alive; for, it must be remembered, a child may breathe and yet be born dead. Experiments have taught us that in a still-born child the forcing of air into its lungs in an attempt at resuscitation will produce the same condition as that of a child who was born alive but breathed only feebly. It is only after all these details have been most carefully observed that the physician may feel warranted in forming a trustworthy opinion. In atelectasis the child may be born alive and exist for some hours, yet the lungs will sink in water, even when divided into small portions.

In those infants who have lived long enough to feed, the presence of food or other foreign substances in the stomach proves that the child was alive at birth, and if death is the result of poisoning, the appearance of the gastric mucous membrane or the usual chemical analysis will reveal the cause of death. It must be remembered, however, that it is possible for an infant, still-born, to have amniotic fluid or other contents of the parturient canal in its stomach as the result of an effort to breathe, the material having been drawn into the mouth during such effort and then swallowed before death ensued.

Death from suffocation is very common in the new-born; it may be due to some malformation, to weakness, to the blocking of the air passages with mucus or other substances, or to the effects of too heavy covering. Where destruction is intended and a damp cloth or other impermeable material is placed over the mouth and nostrils, death will result; and if the act has been done without the employment of undue pressure, the medical witness will be at a loss to state whether the child was born alive or dead, his opinion being possibly in favor of the latter view.

Birth Records.—The medical attendant should write down at the time the exact date and hour of birth, the sex of the child, the state of its development and all characteristic marks, and he should place this record on file for reference. In many legal battles such a record has been of value in determining the right of inheritance and has aided in dealing justice where fraud has been attempted. Male children have been substituted for female, living children for those born dead, and a perfect

child for a monster who would not be recognized as a legal heir.

Insanity.—Under this heading we shall not consider those cases in which the insanity is marked by hallucinations and impairment of all functions, but preferably those in which only a careful study will enable the medical witness to determine whether the patient in question is or is not sane, and those who are feigning insanity.

No definite law can be laid down as to what constitutes insanity; all symptoms must therefore be carefully studied and deductions drawn from them for the benefit of the court.

Persons displaying unnecessary hatred to those about them are often presented for examination as to their sanity, as this characteristic is offered in evidence in case of criminal proceedings against them; but unless it can be shown that there is some impairment of the faculties of attention, comparison, and volition, the individual cannot be adjudged insane. The faculties should be examined when the patient is not conscious of the object of the visit made. Ordinary subjects of general conversation should be used in this examination and mental note made of any and all irregularities, which can be reduced to writing as soon as possible after the examination is concluded. During the examining visit some subject should be introduced which requires that the patient shall write a letter of his own composition which, in genuine cases of insanity, will give evidence of the condition that can readily be demonstrated. Patients of this nature should be repeatedly examined, as many of them present lucid intervals.

Perhaps the most common condition in which the average practitioner is called to testify is that of setting aside a will, the charge usually being made that at the time of execution, or possibly of alteration, the patient was not of sound mind. When attending a case in what appears to be the last illness, the physician should note carefully the patient's mental condition from visit to visit, and he should preserve a record of these observations, in order that he may be able, if called as a witness, to state whether the supposed irregularities were due to a weakened mental condition or to an eccentric disposition.

In the case of criminals for whom is entered a plea of insanity, a careful study of their history and the facts and conditions of the crime committed will usually clear up the medical aspect and enable the physician, when on the witness stand, to be sure of his ground.

A sane person will be found to have a motive for the crime, be it plunder or revenge; he is often assisted in the crime and will at first usually deny guilt, except in cases in which the motive for the crime is notoriety, as in the assassinations of Presidents Garfield and McKinley. An insane person will have no motive, or only a fancied one, for the commission of the crime, and, instead of one victim, as would be the case if the murderer were a sane person, he will often kill several, perhaps those most near and dear, and will make no attempt to cover up his tracks or deny the act.

Life Insurance.—Where life insurance is concerned, the medical witness is of importance in determining—for the satisfaction of the heirs of the deceased, of the company carrying the liability, and of the court, if legal action has been started—as to whether death was the result of natural or of violent means. In the case of a natural death it is important to learn how long the individual had suffered from the disease that caused death, and whether or not there were predisposing chronic pathological conditions existing prior to the issuance of the policy covering the case involved. On the other hand, if death resulted from violence, it is necessary to ascertain whether the cause was criminal, accidental, or suicidal.

Accident insurance having now become an extensive business the attention of the profession is frequently called to cases that require the utmost care in arriving at a definite opinion. Diabetic ulcerations are stated to be the result of trauma (a wound received in a barroom fight or an injury caused by a fall)[1] or a syphilitic ulceration is claimed to be the result of a burn, and so on through the entire list of diseased conditions that produce lesions which can be charged to an accident.

Shrewd criminals often conceive unique plans for defrauding insurance companies, and the medical witness must always be on the alert for such surprises. Post-mortem examinations should always be insisted upon when a case is not absolutely clear.

Partnership.—Agreements are often entered into by members of the medical profession for mutual benefit and a firm name selected. The basis for settlement is decided upon and division made accordingly, but no legal responsibility is assumed by one for the other, and each member of the firm is alone responsible for errors made in his professional work. Should the firm enter jointly into outside investments, they then become liable under the law to the same extent as do the regular commercial unions.

Fees.—The question of fees has ever been a hard one for the medical profession. The courts have ruled that no one is so good a judge as to the number of visits necessary to be made in a given case as the medical attendant, and he can so render an account. In several States fee bills have been enacted regulating the maximum amount to be charged for certain classes of work. As nearly every case—especially those wherein the amount of the bill rendered is claimed to be exorbitant—possesses certain complications, it is not hard for expert opinion to prove to the court or jury that the fee charged is not excessive. By far the most common question that arises in this connection is not the amount, but who shall pay the fee. A prominent Cincinnati surgeon recently sued a corporation for services rendered an employee and lost his case, the court ruling that the defence had proven that the individual who employed the doctor, although he was connected with their concern, had no authority to make contracts, and was simply acting as a messenger for the injured person, and that the patient must be looked to for liquidation of the account.

When answering calls where it is probable that the individual requiring the service will be unable to pay for the same, the physician should ask some one in authority to become responsible. It is not sufficient for a person in authority simply to ask the medical man to assume charge of a case, he must also agree to settle for the service rendered; otherwise liability can be denied and this defence will be sustained by the court. In nearly all sections of the United States this ruling has prevailed where medical men have been called to attend an injured passenger or employee by local agents, conductors, and other minor officials of railway companies. The same ruling applies in cases in which parents have requested attendance upon their children of legal age; the patient being considered liable while the parent is looked upon as a simple messenger without liability. In the case of the wife, legally absent from home, the husband is held to be responsible for medical attention rendered; if, on the other hand, she is not legally absent, she alone is considered responsible.

Consent of Patient.—In cases of injury, or in those in which it has been determined that an operation is necessary, it should always be the rule to obtain the consent of the patient to do whatever is necessary after administration of the anæsthetic. In case the patient is not in a condition to understand, or if the patient is a minor, then the consent of a responsible member of the family or guardian should be obtained. Occasionally one meets with cases in which the individual claims to prefer death to the loss of a limb, and if he still persists in this view after all the facts are set forth, his wish must be respected. It is needless to say that every avenue for a malpractice attack must be carefully guarded either by securing in advance reliable disinterested witnesses or by resigning the case if another practitioner can be found who is willing to assume charge.

Consent procured by misrepresentation has no standing in law.

Mr. Benjamin Vaughan Abbott, in his excellent article

on this subject in the first edition of the HANDBOOK, cites a case of much interest, as follows: "A lady became suspicious that a housemaid in her employ had become pregnant, taxed her with it, and gave her notice of dismissal. She denied it. The lady sent for her family physician and ordered the girl to go to her room and submit to an examination. The girl protested, but went to the room followed by the physician. She objected to each of the doctor's requirements, as to removing her clothing, etc. However, she obeyed, remonstrating all the while, and the usual examination was made, resulting in the doctor being satisfied that the charge was groundless. But the mistress dismissed her, notwithstanding. A lawsuit was brought on behalf of the girl against the physician, for damages for assault. The case was several times discussed in court, with the final result in the physician's favor. The courts considered that although the girl remonstrated, yet as she went to her room, undressed, and lay down to be examined, all without being forced, the examination did not take place in a legal sense without her consent. It was a case of reluctant obedience to arbitrary, wrongful command, as distinguished from a forcible compulsion which she was powerless to resist."

Emergencies.—While there is no definite law covering the rights of the profession at large in emergencies, the courts would no doubt sustain any action necessary for the well-being and safety of the public. Health officers are given a wide latitude in all matters of public hygiene and safety and should always be appealed to if possible.

Relation of Physician and Patient.—The relation of patient and physician is acknowledged by law to be most intimate. Any abuse of this confidence on the part of the physician would in all probability render him liable in a suit for damages. Abbott[2] reports a case from the Michigan courts in which a physician was assessed damages for allowing a non-medical man to be present and render slight assistance at an obstetrical case, notwithstanding the fact that the physician showed that circumstances required his being accompanied by the man in question, and that there was no other protection from the prevailing storm than the room in which the woman was confined.

In damage suits the ruling has been made that the attending physician may testify as to what the patient said regarding the manner in which the accident occurred, it being held that the law in its strict sense refers to those things necessary for the physician to know regarding family history, habits, etc., for the proper treatment of the case, and not to voluntary admissions made during the visit. This ruling would not hold in criminal cases if the patient should admit that a wound had been received while doing a dishonest act. Here the ruling has been made that this is imparted in confidence and must not be revealed under any circumstances. On the other hand, the law will not protect a third party, guilty of crime, but will allow the testimony of the attending physician to assist in conviction. To illustrate, we will consider the case of a young woman dying as a result of criminal abortion. Here all the facts were given the attending physician as a dying statement. This was admissible as evidence to aid in the conviction of those responsible for her condition. In the case of State *vs.* Pierson, the latter was charged with having caused the death of one Withey by the administration of arsenic. In this case the physician who attended Withey in his last illness was allowed to testify as to what he saw and heard. This was sustained by the Court of Appeals under the ruling that the law was to protect the patient and physician in legitimate communications, not to shield criminals.

Wills.—It is not often that the physician is concerned in the drawing of such documents, and it should be avoided if possible, especially if complicated details are to be arranged or the doctor is to be a beneficiary. In cases of emergency it may be necessary for the attending physician to draw up the will, in which case any simple, but clear, form will be sufficient. Have the instrument signed and witnessed by three or more competent individuals and deliver the document into safe hands.

Mark A. Brown.

[1] Taylor's Medical Jurisprudence.
[2] Abbott: REFERENCE HANDBOOK OF THE MEDICAL SCIENCES, Vol V., page 673, first edition.

PHYSICIANS: RELATIVE NUMBER AS COMPARED WITH EXISTING POPULATIONS.—The relative number of physicians in any country or population depends upon many circumstances and conditions, such as the laws governing the practice of medicine, the progress of medical education, the prevalence of empiricism, and many other social conditions.

In some countries the number may be ascertained from the figures of the census; in others, as in Germany, from careful enumerations of the medical profession made by the Government.

In the United States at the present time certain medical directories, issued at frequent intervals, contain this information, with an approximate degree of accuracy.

The following tables present the numbers of physicians per 10,000 of the population in each of the United States in the two years 1898 and 1902:

RATIO OF PHYSICIANS TO THE POPULATION IN THE UNITED STATES IN 1898 AND IN 1902 IN GROUPS.

States and Territories.	Ratio of physicians to the population, 1898.		States and Territories.	Ratio of physicians to the population, 1902.	
California	23.8	More than 20.	California	26.1	More than 20.
Iowa	23.7		Colorado	23.4	
Indiana	21.4		Vermont	21.5	
Vermont	20.8		Indian Territory	20.7	
Ohio	20.3		Oklahoma	20.6	
Illinois	19.3		Missouri	20.3	
Arizona	19.1		Ohio	20.3	
Missouri	19.0		Arkansas	19.7	
Colorado	18.7		Indiana	19.7	
Tennessee	18.6		Maine	18.8	
Massachusetts	18.5		Iowa	18.4	
New Hampshire	18.1		Kansas	18.4	
Maryland	17.9		Illinois	18.3	
New York	17.7		Tennessee	18.2	
Texas	17.5		Maryland	18.1	
Arkansas	17.2		New Hampshire	17.8	
Maine	16.8		Michigan	17.6	
Kentucky	16.5	13.3 to 20.	Massachusetts	17.2	13.3 to 20.
Nevada	16.3		Texas	17.2	
Michigan	16.0		New York	16.9	
UNITED STATES	15.4		Kentucky	16.3	
Connecticut	15.2		Nevada	16.3	
Rhode Island	15.2		UNITED STATES	15.9	
Oregon	14.9		Pennsylvania	15.4	
West Virginia	14.9		Oregon	15.3	
Pennsylvania	14.9		Rhode Island	15.2	
Oklahoma	14.4		West Virginia	15.1	
Florida	14.4		Connecticut	15.0	
Delaware	14.2		Washington	14.9	
Montana	14.0		Delaware	14.7	
Idaho	13.8		Arizona	14.5	
Kansas	13.6		Nebraska	14.3	
Virginia	12.3	10 to 13.3.	Georgia	14.2	
Georgia	12.3		Idaho	13.4	
New Jersey	12.1		Montana	13.2	10 to 13.3
Alabama	11.9		Florida	13.1	
Washington	11.3		Wyoming	13.0	
Wisconsin	11.3		Alabama	12.2	
Louisiana	11.0		New Jersey	12.1	
Mississippi	10.9		South Dakota	12.1	
Utah	10.2		Virginia	12.0	
Minnesota	9.6	8 to 10.	Wisconsin	11.5	
Wyoming	9.4		Utah	10.7	
Nebraska	9.2		Alaska	10.7	
South Carolina	8.7		Minnesota	10.6	
North Carolina	8.5		Louisiana	10.6	
North Dakota	7.8	Less than 8.	Mississippi	10.1	
South Dakota	7.7		North Dakota	9.3	8 to 10.
New Mexico	7.2		New Mexico	8.5	
			North Carolina	8.2	
			South Carolina	8.1	

Allowance has been made in the foregoing tables for increase of population.

Examination of the foregoing table shows that the ratio of physicians in the United States has increased from 15.4 per 10,000 inhabitants in 1898 to 15.9 in 1902.

The ratio had increased in each of 29 States and Territories, and had decreased in 19. Alaska and the Indian Territory are included in the second list, but not in the first.

The States in which either the increase or decrease appears to have been excessive are Iowa and Arizona, with decrease of 22 and 24 per cent. respectively, and Kansas, Wyoming, Oklahoma, Nebraska, and South Dakota with increase of 35, 38, 43, 55, and 57 per cent. respectively.

The map or chart shown herewith was constructed for the year 1898 and presents the ratio of physicians to the population by means of different shadings, black indicating the highest ratio.

The information obtained from these figures must be deemed to be only approximately accurate, since the two essential factors, namely, the directory list of physicians and the census enumeration of the population, with the necessary estimates for intercensal years, cannot be regarded as strictly correct in a rapidly growing country like the United States, subject to the constant change which attends the migration of population, not only from foreign countries to the United States, but also from one State to another.

In general, however, the figures for the larger States, and for the New England, Middle, and Southern States, embraced in all the groups except the first, may be considered to be fairly trustworthy.

and in Porto Rico and the Philippines less than 1 per 10,000.

The relative number of physicians in other countries is generally less than it is in the United States. Prinzing* published the following figures in 1901 for the principal European countries:

Number of physicians and surgeons to each 10,000 inhabitants: In Germany, 5.1; in Austria, 4.1; in Hungary, 2.8; in Italy, 6.3; in Switzerland, 6.1; in France, 3.9; in Spain, 7.1; in Belgium, 5.2; in England, 6.1; in Scotland, 7.7; in Ireland, 5.6; in Denmark, 6.4; in Norway, 5.3; in Sweden, 2.7; in Russia (European), 2.7.

The number of homœopathic physicians in the principal states of the German Empire were as follows:

In Württemberg	30 or 3.7 per cent. of the whole number of physicians.
In Russia	136 or 0.9 of one per cent. of the whole number.
In Baden	8 or 0.9 of one per cent. of the whole number.
In Saxony	15 or 0.8 of one per cent. of the whole number.
In Bavaria	16 or 0.6 of one per cent. of the whole number.

At the last enumeration of physicians in the German Empire, the whole number of homœopathic physicians in the empire was stated to be 240, or less than 1 per cent. of the whole number of practitioners, which was 27,374.

The number of physicians in Germany has increased both absolutely and relatively, from 13,728, or 3.2 per

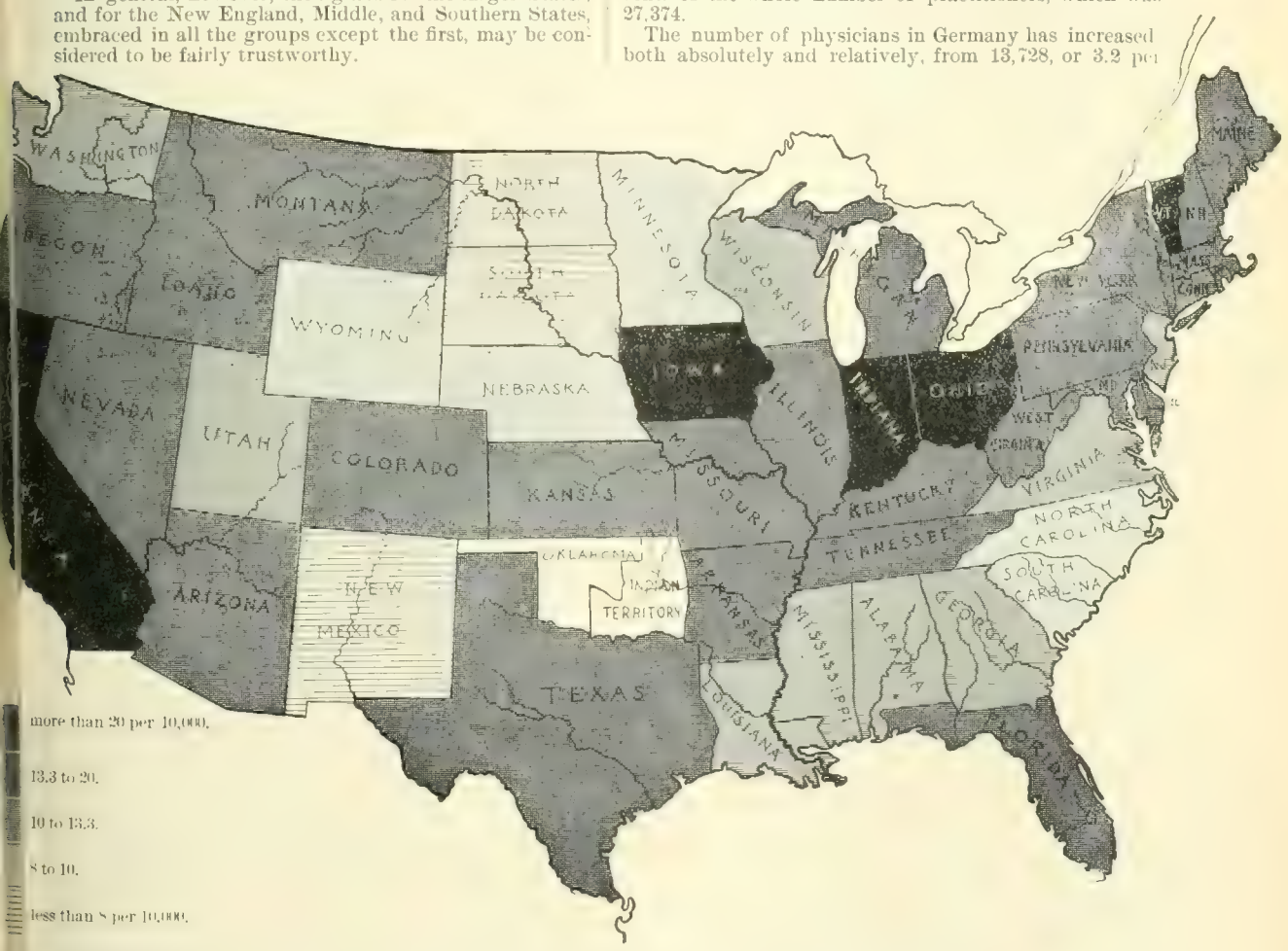

FIG. 5162.—Ratio of Physicians to the Population in the United States, per 10,000 Inhabitants in 1898.

The figures for the Philippine Islands, Hawaii, and Porto Rico are not given in the table, since they can hardly be regarded as valuable for purposes of comparison. The ratio in Hawaii is stated to be 5 per 10,000.

10,000 inhabitants in 1876, to 27,374, or 5.1 per 10,000, in 1900.†

* Zeitschr. f. Socialwissensch., 1901, Bd. 4, Hft. 7.
† Rheinischer Kurier, 1901, No. 415.

In the whole of Prussia there were registered in 1900 16,100 physicians, 956 dentists, and 3,118 apothecaries.*

Prinzing also states that quackery has gained so strong a foothold in Germany as to demand energetic measures for its suppression. Weavers, barbers, shoemakers, and persons of other ordinary occupations are often found practising as physicians.

The relative number of quacks in 1898 in the principal German states were as follows: In Saxony, 16.4 per 10,000; in Württemberg, 5.5; in Prussia, 5.3; in Bavaria, 4.5; in Baden, 2.9; in Hesse, 2.9; in Alsace-Lorraine, 1.3.

The veterinary surgeons in Germany at the last enumeration were 3,813 in number, and when compared with the class of patients whose ills they are called upon to relieve, were found to be in the proportion of 1 to every 1,240 horses and every 5,677 head of cattle.

The proportion of physicians in the cities is, as might be expected, much greater than that of the rural districts. For example in Germany in 1876, in the cities and towns having more than 5,000 inhabitants in each, the ratio of physicians was 7.5 to each 10,000 inhabitants, and in the rural districts only 1.8 per 10,000. These figures had increased respectively to 8.4 and 2.4 in 1898.†

The ratios of physicians in the great cities of Europe and the United States were as follows during the years named: London (1895), 12.8 per 10,000 population; Paris (1896), 9.7; Berlin (1900) 14.1; Vienna (1896), 13.0; Brussels (1897), 14.7; Budapest (1896), 16.4; Madrid (1899), 24.4; New York (1901), 17.1; Chicago (1901), 20.5; Philadelphia (1901), 21.8; St. Louis, 26.3; Boston, 26.8; Baltimore, 23; Cleveland, 21.9; Buffalo, 19.6; San Francisco, 31.5. *Samuel W. Abbott.*

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PITYRIASIS ROSEA.—Pityriasis rosea is a disease of the skin characterized by the development of symmetrically distributed patches, roundish or circinate in outline, slightly scaly and of a faint red color. It is one of the rarer dermatoses. The disease has been described under several names. Pityriasis rosea, the name given it by Gibert, is the one nearly universally used now. It was described by Hebra under the name herpes tonsurans maculosus, and by Bazin under the title pityriasis maculata et circinata.

SYMPTOMATOLOGY.—The eruption occurs in two forms, the macular and the circinate. Probably the first lesion in both forms is a very small pinkish macule or papule which rapidly spreads to form the characteristic macule or patch of the disease. In the macular type the lesions are roundish patches, gradually fading into the healthy skin, of a pinkish color and covered with fine branny scales. These patches vary in size from one-sixteenth to three-quarters of an inch in diameter, and are of a reddish to fawn color. Frequently the periphery of the lesions will show the erythematous color while the centre will be fading.

The circinate type of the disease differs from the macular in that the tendency of the patches to spread peripherally is more marked. In this form the border spreads while the centre fades. The typical lesion of this form, therefore, is a more or less circular patch with a pinkish border and a fawn-colored scaly centre. Adjacent patches of this sort may coalesce and thus form peculiar gyrate figures. These patches do not usually become larger than an inch in diameter. By the time they reach that size the reddish border breaks up and fades out, leaving the characteristic fawn-colored stains of the disease. The lesions are apt to occur in successive crops, so that it is possible to see at one time the minute papules of the beginning of the disease, along with the patches and circinate figures of a later stage of the process. At times the eruption remains papular for the most part throughout its entire course, only a few patches or circinate figures developing.

Brocq called attention to the fact that a single primary patch, usually of large size and situated upon the abdomen, preceded by ten days or two weeks the general eruption, and this observation has been confirmed by other dermatologists.

The extent of the eruption varies very greatly. In some cases it is confined to one or two regions, but most frequently it is widely distributed. It occurs by preference on the front and sides of the abdomen, over the chest and on the buttocks, and on the sides of the neck. It may be universal, but it rarely develops on the face or below the elbows and knees. There is also considerable variation in different cases in the color of the lesions, which at times show an inflammatory red but more frequently a pinkish or fawn color. The eruption usually disappears in from two or three weeks to two or three months, but cases not infrequently last longer, even for four or six months.

The appearance of the eruption is usually preceded by a slight rise of temperature with general malaise, but these systemic manifestations are usually so slight as to pass almost unnoticed. There may be some enlargement of the lymphatic glands. This may be confined to the submaxillary and post-cervical glands. At times also the axillary and inguinal glands show slight painless enlargement. There is slight itching, particularly at night, or when the patient gets overheated, but it is not of severe character and causes little or no annoyance.

ETIOLOGY.—The etiology of the disease is unknown. Like the exanthemata and other toxic eruptions it occurs most frequently in children. It was thought by Hebra to be a mycotic affection, and this view still has its advocates. Its symmetrical distribution, the accompanying slight febrile disturbance, and the character of the eruption seem to indicate that it is closely allied to erythema multiforme.

HISTOPATHOLOGY.—Microscopically the changes found are those of a slight inflammatory process in the skin.

DIAGNOSIS.—The exceedingly trivial character of the systemic disturbances and the duration of the eruption serve to distinguish it from the exanthemata. From psoriasis and widely distributed forms of seborrhœic eczema occurring in small patches, it is distinguished by the lack of infiltration of the patches, the much lower grade of inflammation, and the character of the scales, the fine branny scales of pityriasis rosea presenting no similarity to the coarser scales of psoriasis and seborrhœic eczema. From tinea circinata it is distinguished by its much wider distribution, the rapid development of the lesions, and the absence of the ringworm fungus. It is most likely to be confused with the squamous and circinate syphilides, from which it is distinguished by more rapid development, less scaling, absence from the face and hands, and the absence of concomitant symptoms of secondary syphilis.

TREATMENT.—The disease requires very little treatment. Constitutional treatment should be symptomatic. Certain authorities think they have seen benefit from the use of salicylic-acid compounds. A mild antipruritic dusting powder, or lotion or salve is all that is necessary in the way of local treatment. *William Allen Pusey.*

PITYRIASIS RUBRA.—Pityriasis rubra is a dermatitis, usually subacute or chronic in intensity, in all but the most exceptional cases universal, and characterized by abundant dry desquamation. Other names by which the condition is known are dermatitis exfoliativa (Wilson), pityriasis rubra aigu (Devergie), erythrodermie exfoliante (Besnier). It is a rare disease.

SYMPTOMATOLOGY.—The disease may begin primarily

* R. Wehmer: Medicinal-Kalender, Berlin, 1901.
† Vierteljahrsschrift f. öff. Gesundheitspflege, 1902, vol. xxxiii., Suppl., p. 402.

as pityriasis rubra, or it may develop upon other inflammatory dermatoses. When occurring primarily it may begin in either of two ways. In some cases it begins as a diffuse hyperæmia, which increases until the skin becomes a bright red, and with the increase in redness there is the development of the characteristic desquamation. In other cases it begins as circumscribed red scaly patches. These spread peripherally and new patches form at the same time, until the entire surface becomes involved in the process. In the early stages of the disease the skin is of a bright, hyperæmic red color, which fades on pressure, and the induration is very slight. As the process becomes older the redness becomes of a deeper hue, and in some cases has presented a markedly venous character. There is also at times, even when arsenic has not been used, the development of marked pigmentation in the skin. The true color of the skin is more or less concealed by the abundant grayish scales which cover it. The abundance of this desquamation is one of the most salient characteristics of pityriasis rubra. The scales are dry and grayish in color; at times they are fine, but usually, except on the face, they occur as thin papery flakes. On the palms and soles the horny epidermis exfoliates in large flakes, which may at times amount to masks of the parts. The scales are easily detached and quickly reform. A quart or more of scales may be produced in twenty-four hours, so that they can be collected by the handful from the patient's bed. There is usually very slight induration of the skin, although after the disease has persisted for a long time the skin may become considerably indurated and stiffened as a result of the chronic inflammatory process. Rarely is there any free exudate. Except for perspiration the skin is dry, although a certain amount of weeping and even the formation of bullæ have been described. When we come, however, to cases of this character, accompanied by bullæ and free exudation, the border-line between this disease and pemphigus foliaceus becomes confusing.

There is more or less involvement of the appendages of the skin. The growth of the hair is interfered with and much falling of the hair takes place. At times the accumulation of scales underneath the nails causes them to be raised up and thrown off. Again the nails may become thin and softened and stunted or lost entirely. In some cases the nails become thick and rough and striated. The secretion of sweat is usually much diminished, but there may be an increase on such parts as the axillæ and genito-crural fold. The tongue in most cases is bright red, undoubtedly due to the exfoliation of the epithelium, which is washed away in the saliva.

The subjective symptoms are relatively unimportant. In rare cases the itching is severe, but usually it is of trivial character or absent. The sensation is more apt to be one of tenderness, burning, and stiffness of the skin. The onset of the disease is usually accompanied by a temporary febrile disturbance, which may recur with each exacerbation of the process. Except for such slight disturbances there may be no positive illness, although there is usually an indefinite lowering of the general physical tone, which becomes more marked as the disease progresses. Later on, the patients become anæmic, cachectic, and emaciated, and thus become the ready prey to intercurrent affections. Insanity, and other mental and nervous disturbances have been noted in a number of the cases.

The acute cases are often accompanied by very violent constitutional symptoms, with all the evidences of grave septic or nutritional disturbance. The temperature may range as high as 105° or 106° F. There may be great depression, diarrhœa, rigors, and a typhoid condition, and death may occur in one or two weeks.

Etiology.—The cause of the disease is unknown. It is probable that several conditions, essentially different, present this complex of symptoms. It is rare in children and occurs most frequently after middle life. It is more frequently observed in men than in women. Crocker thinks there is a close relationship between acute rheumatism and gout and pityriasis rubra, eleven out of eighteen cases which he analyzed having shown this relationship. Jadassohn has pointed out the frequency of the association of tuberculosis in some form with pityriasis rubra. It is recognized that pityriasis rubra may supervene upon psoriasis, eczema, and other inflammatory affections. Brocq has seen a severe acute attack brought on by the vigorous application of chrysarobin, and Crocker has seen it follow vigorous inunctions with mercurial ointment and the external use of arsenic. Stelwagon has seen it develop on the extremities after the use of quinine by patients who had an idiosyncrasy as regards that drug. As an exciting cause, sudden chilling of the body has in some cases seemed to have a direct relationship to the development of the disease, and in other cases it has been excited by alcoholic debauches.

Pathology.—Microscopically the disease shows nothing to differentiate it from other simple inflammatory processes in the skin. There are the usual changes of a superficial dermatitis, and when the disease has persisted for a long time there are the connective-tissue changes characteristic of chronic inflammation of the skin. Several efforts have been made to discover central or peripheral nerve changes in connection with the disease, but without definite findings.

Diagnosis.—The involvement of the entire skin, which occurs in all but the rarest cases, the profuse dry desquamation, the slight induration, together with the rapid development, are the prominent characteristics of the disease.

If it is admitted that psoriasis or a squamous eczema could become absolutely universal and of uniform type of eruption throughout, it is possible that they might be confused with pityriasis rubra. It is hardly likely, however, that this ever occurs. A universal psoriasis could be differentiated by the gradual development, the greater induration of the skin, and the thick, silvery white, closely adherent scales of that disease, and the hemorrhagic puncta following the forcible removal of the scales. It is hardly conceivable that an eczema could show a uniform type of eruption over the entire body, such as is seen in pityriasis rubra. Additional points of distinction from eczema would be the yellowish crusts of eczema, the presence of more or less free exudate, less rapid onset, greater induration of skin, more itching, and less evidence of constitutional disturbance.

The two conditions with which pityriasis rubra is likely to be confused are pemphigus foliaceus and pityriasis rubra pilaris. In pemphigus foliaceus there is the occurrence of flaccid bullæ, which, if not seen themselves, at least leave traces of their existence in undermined borders of epidermis and in the excretion of serum and pus, which dries in crusts upon the surface and gives rise to the sickening characteristic odor of pemphigus foliaceus. Pityriasis rubra pilaris does not develop so rapidly as pityriasis rubra, is not so likely to be universal, is accompanied by much greater induration of the skin, and shows the characteristic papules, which are entirely absent in pityriasis rubra. These rough, dry, horny papules, capping the hair follicles and giving the skin the nutmeg-grater appearance, that are seen on the back of the fingers and hands in pityriasis rubra pilaris, are entirely absent in pityriasis rubra.

Treatment.—The patients are made much more comfortable by emollient local applications. The essential thing is to keep the skin thoroughly lubricated. This may be done with vaseline, rose ointment, olive oil, lanolin, or mixtures of these in the form of liniments. The internal treatment is symptomatic, and is directed toward building up the patient's general health. Arsenic and quinine have both been advised empirically without very strong evidence of their having any specific effect. The patients should be carefully protected against chilling, and they do best when they stay in bed. There is little evidence that treatment has any effect except in relieving symptoms. *William Allen Pusey.*

PITYRIASIS RUBRA PILARIS. See *Lichen Ruber Acuminatus*

PONS AND MEDULLA, DISEASES OF THE.—It is a fortunate fact that the occurrence of vascular lesions, such as hemorrhage, embolus, and thrombosis, is rare in the neighborhood of the pons and medulla. They may of course occur in the presence of such a favoring element as cardio-vascular disease, which in turn may be due to a variety of causes, but when they are of any considerable size they are so quickly fatal that a determination of their exact location within the above structures is practically impossible. It is, moreover, not particularly easy, even though the lesion be so small as to be compatible with life, to locate it with absolute definiteness, and this in spite of the fact that the industry, both of the clinician and of the pathologist, has guided us to a remarkably clear comprehension of the physiologic values of the various nuclei, nerve fibres and tracts which lie in and traverse this anatomically complex territory.

In the case of extensive hemorrhage the victim is struck down so suddenly, and unconsciousness supervenes so rapidly that it is impossible to separate the damage to individual nuclei from the general havoc which the lesion entails. Certain features are, however, usually present which indicate in a measure the general situation of the extravasated blood. The respiration, for instance, rather quickly assumes the Cheyne-Stokes character, and this in itself should arouse a suspicion of the intimate relationship between the hemorrhage and the respiratory centre. Conjugate deviation of the eyes is also a fairly reliable indication of ponto-medullary hemorrhage, the eyes being turned toward the side opposite the lesion. The resultant paralysis is apt to be bilateral even though the hemorrhage be unilateral and differs from the flaccid type observed at the outset of an ordinary apoplexy in the tendency of the extremities to assume a degree of rigidity. This rigidity may be accompanied by a recurring shock-like tremor of a rather coarse type. The behavior of the reflexes is not sufficiently constant to be dependable, and there is nothing strikingly characteristic about the pulse and temperature.

In arterial lesions of lesser grades of severity the symptoms may be grouped in a variety of ways, dependent upon their site and extent. A lesion involving the pyramidal tract in the upper pons produces an ordinary hemiplegia, but if it be sufficiently extensive to include the facial nucleus, or even its roots, there usually results a so-called alternating hemiplegia; that is to say, a facial paralysis corresponding to the side of the lesion and a paralysis of the opposite side of the body.

A similar type is observed where the nucleus of the sixth nerve is included in the lesion. In other cases both the abducens and the facial nerves may be involved on the side of the vascular disturbance, and the resulting paralysis may be associated with hemiplegia of the opposite side of the body. Oftentimes the disturbance lies not exactly in the sixth nucleus, but near by in the conjoined centre for the sixth of the same side and the opposite rectus. This produces the conjugate deviation of the eyes away from the side of the lesion spoken of above.

The variety of clinical combinations which may occur in vascular lesions of the ponto-medullary region is relatively extensive. An examination of its anatomy reveals the fact that it contains the nuclei of the larger part of the cranial nerves, nuclei which serve also as trophic centres. It contains furthermore centres governing the respiration and the heart's action; likewise the great tracts and network of fibres which have to do with motion, sensation, and equilibration. The act of vomiting, the secretion of the saliva, and the vaso-motor activities of the body also doubtlessly depend upon centres located in this important region. Nowhere else in the central nervous system are so many important structures in such close proximity; hence it is easy to understand the eccentric grouping of symptoms arising from simultaneous destruction of nuclei and nerve tracts, both sensory and motor.

To attempt to give in detail all the clinical combinations to which acute vascular lesions of this region may give rise would be as fruitless as it is impossible, the element of fortuitousness being too strongly in the ascendant. Generally speaking the onset of trouble is marked by rather severe vertigo, which may be accompanied by vomiting of equal severity. Consciousness is seldom profoundly disturbed, hence the patient is able to observe and give an account of his troubles. These may consist of the alternating hemiplegia above mentioned, or may be further complicated by a more or less extensive loss of sensation, by ataxia of the upper or lower extremities, by difficulty in speech and in swallowing, by diplopia, or by a complete loss of control of the facial muscles which externalize the emotions.

As stated above, it is impossible to construct a semeiology which will fit every case. The point always to be emphasized is the eccentric grouping of symptoms indicating nuclear palsy combined with more or less extensive implications of the motor and sensory tracts.

The prognosis in this class of cases is fairly good as regards life. The damage to the nuclear elements is, however, practically permanent, the resultant paralysis being for the most part of the atrophic type.

Treatment is of little avail except in cases in which syphilis is the etiologic factor.

The medulla may be involved during the course of many diseases of the central nervous system, notably tabes, progressive muscular atrophy, multiple sclerosis, gliosis, and amyotrophic lateral sclerosis. It may also be the seat of tumor, abscess, or tuberculous disease. As none of these diseases can be classed as peculiar to the medulla no further consideration will be given them in this article.

The next disease of essentially medullary origin to be considered is the so-called

Progressive Bulbar Paralysis.

(Labio-glosso-laryngeal [Pharyngeal] Paralysis.)

It is to be classed among the rare forms of nervous disease. Its victims are, in the large majority, found among the aged. A so-called infantile type will be spoken of later. As to its etiology nothing definite is known, hence the usual train of causative factors comes in for mention, namely, exposure to cold, traumatism, mental wear and tear; and even abuse of function of the lips, tongue and palate, although it appears that women are less commonly afflicted than men.

Symptomatology.—The first thing that attracts the patient's attention is an unwonted fatigue after talking for any length of time, with a restricted ability to enunciate certain syllables. The initial disability lies, as a rule, in the articulation of the lingual consonants, *l*, *r*, *n*, and *t*. The tongue can at first still be protruded, but not to the normal extent, and there may be a difficulty in securing its proper apposition to the roof of the mouth for sounding the linguo-palatine consonants *t* and *d*. Up to this time the continuous sibilant *s* may be pronounced. With the increasing weakness of the lips whistling becomes impossible and there is an inability to utter the sounds in which the lips are chiefly concerned, such as *o*, *u*, *b*, *p*, and *m*. So imperfectly are the lips brought together and so sluggish is their separation that the labial explosives *b* and *p* degenerate into *m* and *u*. Finally weakness of the palate fails to shut off the nasal cavity, and a part of the expiratory air stream escaping through the nose gives a nasal quality to the voice, *b* and *p* sounding as *mb* and *mp*.

At this stage of the disease dysarthria is fully established. Words are run together and indistinctly articulated, with an intonation of a decidedly nasal quality. Single words may still by special effort be brought out clearly, but sustained speech of any clearness is impossible.

Either at this time or more commonly after the disease has been established a few months the patient experiences a difficulty in swallowing. Only by great effort can food be carried back through the pharynx to the

œsophageal opening. Fluids are constantly regurgitated through the nose, and at times are inhaled into the larynx causing choking and paroxysms of coughing. Ultimately neither fluid nor solid food can be successfully swallowed. Chewing also becomes progressively difficult.

Finally both phonation and respiration become involved. The voice is weak and monotonous and lacks modulation. Hoarseness may develop and go on to complete aphonia. Toward the end respiration becomes labored, and not uncommonly severe attacks of strangulation occur.

Examination of the larynx shows in the beginning nothing abnormal; later, paresis of the adductors is obvious. The masticatory muscles betray their weakness by imperfect closure of the jaw and restricted lateral movements of the same.

Bulbar paralysis is of the degenerative type. Atrophy is, however, not an early symptom and almost never keeps pace with the paralysis. It is usually first observable in the tongue, which becomes lax and feels flabby and spongy; the fibrillary twitching is very striking. Ultimately the organ undergoes a marked grooving and furrowing, and its total volume is much diminished. The lip muscles are rarely affected until late in the course of the disease. They then become thin and toneless. The muscles of the jaw are only rarely markedly wasted, although a fibrillary twitching is not infrequently observed in them at an early stage.

The electrical excitability of the diseased muscles is never greatly altered. Late in the course of the disease there may be some quantitative change to faradism, but examination is never very satisfactory.

When the disease is far advanced the expression of the face is very characteristic and striking. The mouth is open, the lower lip sunken; and drooling is constant. The fixed and expressionless lower part of the face contrasts strangely with the still mobile muscles of the upper face and eyes, which alone afford mimic externalization of intellectual activity. The patient is very emotional and cries easily, but even then the mouth is but little discomposed, whereas the respiratory muscles are thrown into a sort of spasm to which is sometimes added a peculiar respiratory stridor. The shrunken, furrowed tongue lies motionless on the floor of the mouth, articulation is almost annihilated, and the feebly mumbled speech incomprehensible. The respiratory movement is hurried and the pulse may run as high as 140 per minute. Emaciation is very marked.

The above symptomatology develops on the basis of a paralysis of cranial nerves which are purely motor, and there is never implication of nerves which are sensory or sensorial. Curiously enough, however, in certain cases there is to be observed a peculiar heightening of tendon reflex irritability in the facial and masticatory muscles.

Diagnosis.—Bulbar paralysis has so many features that are peculiar that its differentiation from other affections of the medulla should present no special difficulties. The gradual character of its onset and development, its practical restriction to persons of advanced age, the symmetrical implication of purely motor nerves with absence of sensory and sensorial disturbances, and the association of paralysis with atrophy are all factors which serve to crystallize out the disease from other affections of the same region. The features which further distinguish it from acute bulbar paralysis and from the pseudo-bulbar form will be considered later. Tumors of the medulla involve all structures in their neighborhood; hence, sensory nerves suffer as well as motor; furthermore tumors produce the usual train of symptoms characteristic of a general increase of intracranial pressure.

Pathological Anatomy.—The essential morbid change in bulbar paralysis is a progressive decay of the motor nuclei of the facial, hypoglossal, and glosso-pharyngeo-vago-accessory, and occasionally of the trigeminal. The ganglion cells of these nuclei lose their processes, shrivel, and gradually disappear. The intranuclear reticulations and the intra- and extrabulbar roots undergo the same destruction, the change in the latter being sufficiently marked in certain cases to be obvious macroscopically. In some cases the pyramidal tracts are involved.

Prognosis.—The disease is, for the most part, steadily progressive and invariably ends fatally. Its duration varies from one to three years. Remissions rarely occur, although in any case there may be protracted periods during which there appears to be no advance in the symptoms. In quickly progressing cases the disease may run its course in less than a year. Death usually ensues by reason of asphyxia, bronchitis, inhalation pneumonia, inanition, or some intercurrent disease.

Treatment.—Many drugs have been tried, but none is of any special value. Strychnine in gradually increasing doses, arsenic, nitrate of silver, and the iodides are among those most strongly recommended. Forced feeding should be instituted early in the attempt to keep up the nutrition, and later, when dysphagia is established, the food should be introduced artificially into the stomach in order to avoid the very imminent danger of inhalation pneumonia.

A galvanic current of two or three milliampères passed from one mastoid to the other is recommended by Oppenheim.

Vocal gymnastics may be tried in the effort to improve the speech.

The Hereditary (Familial) Type of Progressive Bulbar Paralysis.—A few cases of a peculiar hereditary form of progressive bulbar paralysis have been observed among members of the same family, usually among the offspring of consanguineous marriages. The victims are practically always true degenerates. The peculiarity of the disease in these cases is that it usually affects the upper facial territory first and its effects are most marked in this region, ophthalmoplegia, especially ptosis, being associated with the bulbar phenomena. These latter do not differ from those observed in the ordinary form.

The paralysis is in most cases of the atrophic type and is associated with partial reaction of degeneration.

In 1895 Oppenheim described an infantile form of pseudo-bulbar paralysis. It was observed by him in connection with cerebral infantile diplegia, and consisted of a bilateral paralysis or paresis of the muscles of the tongue, palate, pharynx, and larynx, which gave rise to the characteristic dysarthria, dysphagia, etc. The paralysis was associated with spastic athetotic movements of the affected muscles. Atrophy and fibrillary twitching were absent.

Oppenheim considers the pathologic basis of the disorder to be a bilateral disease or a developmental defect in the central convolutions.

The Acute (Apoplectiform) Type of Bulbar Paralysis.—*Symptomatology.*—Certain cases have definite prodromes, such as pressure in the head, ringing in the ears, vertigo, sleeplessness, and spots before the eyes. The main symptoms develop suddenly. Intense vertigo or even a genuine apoplectic shock with complete loss of consciousness may usher in the attack. Vomiting may accompany the vertigo. In a few cases general convulsions of an epileptiform character have been observed.

Almost immediately after onset a labio-glosso-laryngeal paralysis is found in full development. This is manifested by characteristic dysarthria, dysphagia, etc. Although the paralysis is bilateral it rarely affects the two sides equally. In the majority of the cases the extremities are also involved in the same varying degrees. There may be paralysis of both arms with simple weakness of the legs, or there may be simple hemiplegia, the latter usually on the side opposite to that on which the bulbar nerves are most involved. The onset of all these symptoms may be less sudden, a few days or even a week being required for their full development.

Dyspnœa and even Cheyne-Stokes respiration, with marked increase of the pulse rate, may be present early and may last for a very long time.

Various sensory disturbances are not unusual, and the patient may complain of painful paræsthesiæ in some parts of the body or extremities.

The expression of the face is characteristic; more so in

fact than in the early stage of the chronic type of bulbar paralysis, because the disease renders the facial muscles fixed and expressionless in a very short time.

The paralysis of lips, tongue, and soft palate is naturally not often associated with atrophy—first, because this phenomenon requires time; and, second, because it is the supranuclear part of the nerves which is usually affected. The nucleus itself may be directly affected, though rarely, and in such cases the characteristic atrophy with electrical changes may be found in the affected muscles.

The symptomatology is much more variable than in the chronic bulbar form, and naturally varies with the extent and seat of the lesion. The same eccentric grouping of bulbar nerve paralysis, with paralysis or paresis and sensory disturbance in the trunk and extremities spoken of under vascular lesions of the bulb in general, is to be expected.

Pathological Anatomy.—By far the commonest cause of the acute form of bulbar paralysis is thrombosis with softening. Both hemorrhage and embolism do occur, but with nothing like the same frequency. Polioencephalitis inferior acuta may determine the symptoms above described, and like symptoms are also ascribed to the pressure of a dilated atheromatous basilar artery.

Certain authors have observed the occurrence of an acute bulbar paralysis associated with weakness of the extremities during the course of typhoid; sometimes with a fatal outcome. In the latter cases streptococci and other organisms were found in various parts of the central nervous system without any very marked histological changes.

Prognosis.—Death may result, in very acute cases, within a short time from inhalation pneumonia or cardio-respiratory paralysis. In less severe cases the symptoms are slowly regressive and may gradually disappear, although restoration of function is seldom absolute in all the affected parts.

Treatment.—In cases suspected to be of syphilitic origin the prompt and free use of specific medication is demanded. Otherwise treatment should in the main follow the lines indicated in the therapy of cerebral vascular lesions in general. In the cases which arise in the course of an encephalitis of the ponto-medullary region antiphlogistic and derivative measures are appropriate. Very large doses of calomel may serve a useful purpose even in cases not syphilitic.

It is very important to make every effort to keep up the nutrition from the beginning. As paralysis of the muscles of deglutition may be absolute even from the outset, artificial feeding often becomes indispensable. In the later stages of surviving cases electricity may prove useful.

Labio-glosso-laryngeal Paralysis of Pseudo-bulbar and Cerebro-bulbar Origin.

In very rare cases after a patient has experienced a number of minor apoplectiform attacks a condition resembling the labio-glosso-laryngeal paralysis of bulbar origin, without any implication of the bulb itself, may result.

The pathologic substratum of such cases is a diffuse atheromatosis of the cerebral vessels, which causes a gradual destruction of the cortical representations of the facial, hypoglossal, and motor trigeminal nerves.

To produce a fairly complete analogue of the genuine bulbar type both cortices must undergo considerable destruction in the regions above indicated, with secondary changes in the cortico-bulbar projections. As these changes are all distinctly supranuclear, atrophy and electrical changes in the affected muscles are wanting.

Clinically, while the above picture is in the developmental stage, the patient is observed to have a series of mild shocks which differ in nowise from the ordinary. It is only when the cumulative effects of these various shocks are manifest in a bilateral paralysis or paresis of the muscles of the face, tongue, and jaws with accompanying disturbance of speech, swallowing, etc., that the resemblance to the bulbar paralysis begins. Even then the likeness is not complete, since severe disturbance of the respiration and of phonation is ordinarily absent.

The mental state of such patients differs markedly from that observed in the genuine form of bulbar paralysis in that some type of psychosis, or even dementia, is usually present. So-called bulbar crying and laughing is, on the other hand, commonly present, and may be very marked.

The paralysis is not necessarily limited to the face and tongue areas, so that hemiplegia or diplegia may be present.

A further type—the cerebro-bulbar—described by Oppenheim, differs from the above only in the fact that with the cerebral arterial break-down is associated a similar condition in the bulb. The lesions are never large and the bulbar symptoms are of gradual onset.

Symptomatically, bulbar phenomena are found associated with marked mental deterioration. Both bodily and mentally the patient is in a most deplorable state. With the usual disturbance of speech, mastication, and deglutition is associated spastic paralysis of the extremities on one or both sides. Attacks of dyspnœa and Cheyne-Stokes respiration either come on spontaneously or result from excitement, from paroxysms of spasmodic hiccough, or from attempts at motion. The optic nerves may undergo neuritis with consequent atrophy. The bladder and rectum may or may not be involved.

The prognosis in both the pseudo-bulbar and the cerebro-bulbar forms is very grave, although life may be prolonged for a considerable period of time.

The treatment recommended is that already described elsewhere.

Asthenic Bulbar Paralysis.

(Myasthenia Gravis Pseudoparalytica.)

To Erb (1879) is due the credit of calling attention to a symptom complex which so closely simulated that about to be described under asthenic bulbar paralysis that it must be considered its nosological analogue. It was not, however, until the appearance of Oppenheim's case in 1887 that this singular disease began to attract the attention which has been increasingly accorded to it up to the present moment.

Etiologically, little or nothing definite is known about it beyond the fact that it appears to result from the action of some toxic agent upon a congenitally predisposed nervous organism. Its association with tumors of the mediastinum and of the thymus gland has been noteworthy in specific instances. The predominance of the disease in early life is striking, but persons of advanced years are by no means exempt.

Pathology.—Up to the present time the most searching anatomic investigations have failed to reveal any organic changes in the medulla, bulbar nerves, or muscles. Congenital nervous defects and peculiarities have been observed in connection with certain cases, and a certain amount of stress has been laid upon the same as regards their morbid value, but it remains extremely doubtful if such stress has been rightly placed. The disease, in last analysis, appears to be a true neurosis.

Symptomatology.—This comprises the usual dysarthria, dysphagia, and masticatory weakness with their associated palsy of the lips, tongue, palate and jaw observed in the ordinary types of bulbar paralysis. Added to this is a paralysis of the upper part of the face with imperfect closure of the eyelids. The paralysis also extends to the trunk and extremities, and attacks of dyspnœa are frequent. In a certain number of cases the involvement of the eye muscles, notably ptosis, is the earliest and most striking symptom. Atrophy and reaction of degeneration in the affected nerves and muscles are absent throughout the entire course of the disease regardless of its duration.

Jolly in investigating the behavior of the affected

nerves and muscles to electrical stimulation observed a peculiarity which he designated "myasthenic reaction." He found that where a tetanizing faradic current was applied (either to nerves or muscles) at intervals of a few seconds, the muscular contraction grew progressively weaker and gradually vanished completely, but that the muscle regained its irritability after a short rest. He further found that if the current were passed through a muscle without interruption for the space of a minute or even less, the muscular contraction gradually died away, but was again obtainable by the same sort of stimulation after a minute's rest.

Analogous phenomena have been observed in voluntary attempts to use the muscles of the jaw or extremities. A patient may take one bite of an article of food and then be totally unable to bring the jaws together with any force, but after resting a while may regain enough strength to chew for a few moments.

The course of the disease is very peculiar. The complete development of symptoms may require many months, although in certain cases the time required has been much briefer. Remissions are common, and the full development of symptoms may be followed by a regression, but so treacherous is the malady that when recovery seems fully established, there may be a fresh outbreak of the most rapid character and the symptom complex again be complete in a startlingly short time. Intercurrent attacks of dyspnœa and tachycardia and febrile movements are common.

The disease has on the whole so many peculiarities that differentiation is not difficult. The combination of bulbar symptoms with weakness of the muscles of the trunk and extremities, the frequent involvement of the external ocular muscles (manifested mainly by ptosis), the retention by the affected muscles of their normal volume, the absence of reaction of degeneration in the presence of the peculiar "myasthenic reaction" mentioned above, the characteristic tiring of affected muscles on voluntary motion, the lack of definite sensory and sensorial disturbance, the absence of mental weakness and disease, and the complete lack of any tangible pathologic substratum in the brain, nerves, or muscles unite to form a clinical and anatomical picture that is *sui generis*.

The Prognosis is always serious. Nevertheless the most alarming cases may end in complete recovery. Recovery is, however, never assured until there has been a freedom from symptoms for a period of many months, to the present time the majority of cases have terminated Up fatally.

Treatment.—The proper care of this type of bulbar paralysis requires unusual skill. A complete rest treatment, such as is followed in the severest form of neurasthenia, should be carried out in bad cases to the minutest detail. The patient should be allowed to do almost nothing for himself, even to swallowing food, which, by the way, should be selected so as to combine the maximum of nourishment with the least tax upon the digestive organs. Even the use of the stomach tube for artificial feeding is not devoid of danger, as its introduction may induce fatal suffocation. If mastication can be permitted with safety in a given case, care should be taken to allow the patient to rest between mouthfuls.

The drug treatment consists in the administration of tonics. In certain cases the preliminary production of diaphoresis has been beneficial. Against the use of electrical stimulation it cannot be too strongly cautioned.

Joseph W. Courtney.

PRESCRIPTION-WRITING.—A medical prescription is a written order to the pharmacist to take certain quantities of certain medicines, deal with them in certain pharmaceutical ways, "put up" the product in certain form for dispensing, and label the package with certain directions for use. Correctness in prescribing, therefore, relates to the three several matters of the *selection of the ingredients* or *composition* of the prescription, the *fixing of quantities* or *computation* of the prescription, and the actual *writing of the order* in technical style, or *expression* of the prescription. These several topics will be considered *seriatim*, in the order named.

I. The Composing of a Prescription.—Assuming that a prescription is intended, as always should be the case, to fulfil a single therapeutic purpose only, then the first point that presents is whether, under the circumstances of the case, a *single* medicine of the appropriate kind should be prescribed, or a *team* of such medicines. As regards this point, no general rule can be laid down—the matter will depend partly upon the nature of the therapeutic indication, and partly upon the respective peculiarities of the individual drug and the individual case. Thus to provoke *emesis*, a single drug is commonly prescribed; to excite *diuresis*, a team; while for *purging* the medicine will be single, if it be castor or croton oil, but multiple, if the selection be from among the resinous cathartics. The advantage of a team of similar medicines in prescription may be, on the one hand, a more *effective*, or, on the other, a more *kindly* accomplishment of the specific purpose in view, or it may be both possibilities combined. Thus, by a wise association in prescription of allied drugs, a maximum of therapeutic effect is attainable with a minimum of by-derangement. Having fixed upon the active member, or team of members, of the prescription, the next point is whether the medicinal working of the same may not be made even more effective or more kindly than would otherwise be the case, by the further addition to the prescription of some special substance. Such increase in both lines—effectiveness and kindliness—may result by a chemical action upon the drug, on the one hand, or by a medicinal impression upon the system of the subject, on the other. Thus, as an instance of the working of a chemical action, stands the fact that the efficacy and kindliness of operation of a dose of *salicylic acid* are both enhanced by the addition to the acid of a solution of a sodic carbonate, whereby the salicylic acid, which under its own form is both insoluble and irritant, becomes the more soluble, and at the same time far less harsh, body, sodium salicylate. As instances of an associated medicinal impression by an unrelated drug affecting the operation of the active member of a prescription may be cited the rather mysterious enhancement of the diuretic action of digitalis by the associate action of calomel, and the neutralizing of the griping of the rougher cathartics by the associated antispasmodic action of the pungent volatile oils, or of neurotics, such as belladonna or hyoscyamus. In the category of additions to a prescription for the purpose of enhancing *kindliness* of operation, belong *flavoring* substances. For an agreeable, or, at least, a not offensive potion, is not merely *pleasanter* than an ill-tasting one to swallow, but is also, by the very reason of non-offensiveness, far less likely than a nauseous dose to destroy appetite or derange digestion. The art of prescribing pleasant mixtures is therefore one of genuine advantage to the patient, as well as to the prescriber! Agreeability of taste is, of course, far more important in the case of fluid than of solid mixtures, and is attained, in the case of fluids, in part by wisdom in the selection of the active member of the prescription, and in part by the addition to the prescription of *sugar*, or of *syrup*, or of preparations of the more pleasantly flavored *aromatics*. Lastly, in composing a prescription, comes the thought of a possibly necessary substance to give *volume*, or, in the case of a powder or pill, to give *form*, or, in the case of a fluid mixture, to serve as a diluent, or as a solvent. The character and relative proportion of such a member of a prescription will vary so greatly in different cases, that no general rule affecting the selection of vehicles can be formulated. Members of a prescription for the several purposes named are commonly referred to as, respectively, the *basis*, the *adjuvant*, the *corrigent*, and the *excipient*, or *vehicle*, of the prescription. In the association of different substances in a prescription, no matter what the purpose of the several ingredients, regard must always be had for the mutual *chemical* relations of the things so brought into mutual contact, lest undesirable

reactions take place in the compounding (see *Incompatibility, Medicinal*).

II. The Computing of Amounts in Prescriptions.—The first point in the matter of amounts in prescriptions is, in general, *not to order more of the medicine than present prognosis seems to call for*. Not unnaturally, the laity instinctively argue that the remedy should fit the case in *measure* as well as in *mode*, and hence, that an excess of medicine in the prescription is *prima-facie* evidence of a deficiency of skill on the part of the prescriber. They, furthermore, naturally object to the *paying* for the superfluous. Apart from these considerations, there are also many and obvious objections to a course that leaves half-used parcels of medicine to accumulate in a house, at the risk of inappropriate application on subsequent occasions, at ignorant hands. Hence, in cases in which an exact forecast of the amount of a medicine likely to be required is impossible, it is wiser to order no more than will surely be within bounds, letting the prescription be renewed if the amount prove too little. Assuming due regard to be paid to this principle, then the determination of amounts in a given prescription proceeds, by theory, thus: the amount of *basis* will be the product of the two factors, *quantity of dose* and *number of doses* required, and the several amounts of the other ingredients will be deduced from the amount of the basis, in accordance with the respective requirements of relative proportion. In putting this theory into practice, however, the important consideration has to be regarded, that quantities must be such as can conveniently be expressed in terms of the system of weight or of measure employed in the prescribing. This consideration determines, in general, the use of *round numbers*, and, in particular, of *such* round numbers as best conform to the relation between denominations in the particular system of weight or of measure followed in the prescription. For example, in general, no prescriber would fix a dose to be expressed by such a number as *one and one-tenth*, whether referring to grains or grams, nor would he ever estimate upon an aggregate of such an awkward number of doses as *seven*, or *eleven*, or *nineteen*, or *twenty-three*. And, for example again, in particular, the prescriber by the *apothecaries'* system of weight or of measure, recognizing the generally *duodecimal* ratio of the denominations of these scales, instinctively proportions the numbers of his prescription on a *duodecimal* basis. His ratios, that is, are as one to some one of the numbers 2, 4, 6, 8, 12, 18, 24, 60, 120, 180, 240, 480. On the other hand, if the *metric* system be the system followed, the *decimal* basis of this system almost of necessity entails the use of decimal ratios in proportioning amounts in prescription. Quantities are in this case fixed upon that are to each other as one to some number of this series of numbers: 2, 5, 10, 20, 25, 50, 75, 100, 200, 250, 500, 1,000. This fundamental difference in the figures to be used in working by the metric system as compared with the apothecaries' is a point very commonly overlooked by novices, in this country, in the art of prescribing by metric denominations. Because already fixed in the duodecimal habit through previous practice with the apothecaries' system, such novices are apt to compute in *duodecimal* ratios quantities which they then set down in terms of *decimally* related denominations—a proceeding wherein theoretical stupidity begets, as it should, practical disaster. For, by this proceeding, as it is hardly necessary to point out, there is wholly missed the one point of advantage which the metric system has to offer, namely, ease of computation by *decimal ratios*. A medicine, then, whose dose in prescription by apothecaries' weight is taken at *one grain*, is—or should be—in prescribing by metric weight, taken at *five* centigrams, and not at the *six* centigram amount by which the American metric prescriber, translating from terms of apothecaries' weight, so commonly figures. As well might an original metrician—to coin a convenient word—who essays a prescription by the apothecaries' system, first fix his dose, by his old metric habit, at five centigrams, and then, blindly insisting on exactly that quantum, despite its unsuitableness to the foreign system of weights, prescribe in grains on the absurd basis of a *seven-eighths-grain* dose!

Such are the essential points of the theory of computing prescription amounts, and having due regard to these points, the prescription of *solid* mixtures for make-up into pills, powders, troches, suppositories, etc., is easy enough; but in the prescription of *fluid* mixtures many additional considerations enter into relation, as follows: In the first place, although it is not essential, yet it is elegant, and hence customary, to have a prescribed mixture aggregate *just a bottleful* of some one of the sizes of the medicine phials of the shops. Regard must therefore be had to the several sizes of such bottles. In the United States medicine phials are made of capacities conforming to *apothecaries' measure*, which capacities are severally as follows: *one, two*, and *four fluidrachms*, and *one, two, four, six, eight*, and *twelve fluidounces*. This fact of the conformity of medicine bottles to apothecaries' measure, makes, in this country, the prescribing of fluid mixtures readier by the apothecaries' than by the metric system. Phials for metric prescription should be of the natural metric capacities, severally, of *twenty-five, fifty, one hundred, two hundred*, etc., *cubic centimetres*.

The second special point affecting amounts in the case of fluid mixtures relates to the case of solids in solution, the point being the physical fact that, in dissolving a solid of a given measure in its condition of dry powder *does not augment the volume of the solvent by the full amount of such measure*, but, on the contrary, increases such volume so little that, in the ordinarily comparatively weak solutions used as medicines, the increment can safely be disregarded in the estimation of amounts for prescription.

The third point relates to the system by which, in a given case of a fluid mixture for internal giving, the *individual doses are to be measured*. This consideration does not obtain in the case of solids, since, in such case, doses are defined by a stated number of pills, powders, or troches—are, that is, already apportioned by the apothecary. But in the case of a fluid mixture, the medicine is necessarily dispensed in bulk (except when put up in capsules), and doses must be measured out by the administrator at the bedside. The point then presents itself of practical bearing, whether, in a given case, the dose is to be measured by a method of precision—by use of a graduated pipette, if the dose be quite small, or of a graduated vessel if of ordinary or large dimension—or whether the determination is to be by the conventional *drop* on the one hand or *spoonful* on the other. If a graduate is to be used, then the point now in question does not present itself; but if the *drop* or the *spoonful* is to measure the dose, then the consideration arises, in the apportioning of amounts in prescription, of the respective actual *dimensions* of these variable measures, under the conditions obtaining in the individual case. As regards the *drop*, it must be remembered that this measure varies in dimension, not only according to the viscosity and specific gravity of the fluid dropped, but also according to the *shape, extent*, and *character* of the surface from which the drop delivers itself, and even, furthermore, in the case of drops delivered from a phial, according to the *degree of fulness of the bottle* on the occasion of the dropping. A bottle with a flanged mouth, such as the ordinary medicine phial, yields, with the same fluid, a comparatively large drop when full or nearly so at the dropping, and a comparatively small one when at least half empty, the difference in the respective drop dimensions in the two instances being even as considerable as that between the numbers five and three. The reason for this difference in size of drops is that, from a full bottle, the contents begin to run out when the bottle is but slightly tipped, and accordingly, because of the position of the free edge of the lip, the nascent drop creeps into the re-entrant angle formed by the under surface of the lip and the side of the neck, and there has a chance to grow to a comparatively goodly size before gravity determines the fall. On the other hand, a phial half empty must be tipped to the horizontal before the

contents can run out, in which position the narrow rim of the lip points directly downward, and so presents but a small surface area for the fluid to cling to. Under these circumstances the fall will necessarily be in comparatively small drops. As regards the *spoonful*, it must be remembered that this measure, like the drop, is subject to variation, so that, in the case of prescriptions containing powerful medicines, amounts should be calculated on the basis of the *maximum capacity of the measure*. Whatever, then, may be the variation from the calculated dose in actual mensuration, will be on the safe side of a *shortage* instead of a possible *excess* of amount. Now a given spoon will naturally hold more of a *viscid* than of a *thin* fluid, and, in practical mensuration, will more readily hold its full complement when the fluid is poured *into* it, as from a bottle, than when the spoon is made to dip up the fluid from an open vessel. Hence, in the case of a *syrupy* mixture, with the dose to be taken *directly from the phial*, the conditions obtain where the spoonful will be at its maximum; while, on the other hand, in the instance of a thin watery dilution standing in a tumbler, with the dose to be dipped up by means of the spoon, the measure, although the same in name, may be very different indeed in fact. Another point, which should thoroughly be understood, relates to the size of the average spoon of to-day as compared with the spoon of the same denomination of two generations ago. Coming down from our ancestors is the estimate of the *tablespoonful* as the measure of half a fluidounce, or 16 c.c., and of the *teaspoonful* as that of a fluidrachm, or 4 c.c. These alleged equivalences, true of the average of spoonfuls of former days, are still handed down as present truth from teacher to student, and so come to be almost universally applied in prescription calculations. If, however, the reader will take from any chance pantry a sample of the average commoner kind of teaspoon, such as is generally relegated for service in the nursery, and will provide for himself an accurate graduate and a phial of water, he can learn for himself, in two minutes, the fact that the teaspoonful will run much nearer *six* to the fluidounce than the traditional *eight*—will equal the quantity of *five* rather than of *four* cubic centimetres. And, by the same token, the average tablespoonful of our own present spoons is of the dimensions of *three* rather than of *four* to the two-fluidounce measure—of *twenty* rather than of *sixteen* cubic centimetres. And indeed, in the case of thick fluids, such as strongly syrupy mixtures, or a fixed oil like castor oil, where also the fluid is poured into the spoon, the spoonful will considerably exceed even these larger estimates. In view of these facts, this writer, in his teaching, has always advised for prescription purposes the estimate of the equivalence of the teaspoonful as at 5 c.c., or at the rate of six to the fluidounce; and of the tablespoonful at 20 c.c., or at the rate of three to two fluidounces—six to four fluidounces.

By basing calculations on such assumed equivalences, any error in actual mensuration will be, as it should be, in the direction of a measure smaller rather than greater than intended. Furthermore, it is a happy fact that these equivalences give numerical relations far handier for purposes of calculation than the older estimates. In the case of the metric values, it goes without saying that for computation in decimal denominations, the numbers *five* and *twenty* are much more convenient for expressions of respective unit quantities than the numbers *four* and *sixteen*. And in the apothecaries' system the proportion of six to the fluidounce permits of a greater number of easily calculated combinations than the time-honored eight to the same measure, as is shown in the tables below.

A fourth consideration affecting the estimation of amounts in the prescription of fluid mixtures, obtains in the prescribing of a solid to be borne in solution in an inert fluid menstruum, the point being the matter of the proper proportion between solid and solvent. Of course, in the first place, the proportion must be compatible with the solubility, in the selected menstruum, of the given solid; and, also of course, in the second place, if the dose is to be diluted extemporaneously for the taking, the concentration of the prescribed solution may be to any degree so compatible with solubility. If, however, as so often is the case, the prescription purposes a solution fit for direct administration without further dilution, then the consideration of *taste* enters into relation. An over strong solution will be rough to the taste, and may also be irritant or even corrosive to the alimentary mucous membranes; while, on the other hand, if the solution be inordinately weak, the volume required for the carrying of a proper dose of the dissolved basis may be inconveniently large. Of course, in this matter the individual peculiarities of the constituents of a given prescription will require individual consideration; but, in a general way, the truth obtains that the *teaspoonful* is best made the carrier of not more than—in convenient round numbers of the respective systems of weight—*twenty-five centigrams*, or *five grains*; and, similarly, the *tablespoonful* of not more than, respectively, *one gram*, or *twenty grains*, of a solid in solution. In the case of fairly bland substances, whose solubilities will at the same time permit, twice these quantities may be permissible; but such proportion should not be exceeded.

From this presentation of points affecting the prescription of fluid mixtures, it appears that, in cases in which it is expected that the whole bottleful is to be used, the estimate of amounts must harmonize a trio of conditions as follows: (1) The total must be just a bottleful; (2) it must aggregate *about* the number of doses therapeutically indicated; and (3) at the same time the amount of the active basis, while being such as to yield the proper strength of solution, must also be such as to admit of ready expression in terms of the system of weight or measure employed in the writing. In the use of the metric system this triple harmonization presents no difficulties, for the simple reason that since *any* amount is equally easy of expression by this system, it is only necessary to harmonize the first two considerations, letting the amount of active basis required foot up to what it will. Thus, for instance, let it be supposed that an indication seems to call for a medication three times a day for a few days; then all it is necessary to remember is that, if the active basis be one of small dose such that a teaspoonful is the more convenient carrier, a *fifty cubic centimetre* aggregate will fulfil the conditions of an even bottleful on the one hand, and about the requisite number of doses upon the other (ten teaspoonfuls, reckoning the teaspoonful at 5 c.c.). Then the individual dose of basis may be taken unconditionally by the therapeutic indication—it may be fixed at one, two, three, four, five, six, seven, eight, nine, ten, or any odd number of centigrams, and the expression of the aggregate will be equally easy, such aggregate being simply ten times the quantity for the individual dose, respectively, as follows: 0.10, 0.20, 0.30, 0.40, 0.50, 0.60, 0.70, 0.80, 0.90, 1.00 gm., etc. Similarly, if the case be one where a *tablespoonful* will be the more convenient measure for the dose, then a *two hundred* cubic centimetre volume will again yield ten doses (about the number indicated) of the selected dimension, and once more the individual dose of basis may be what it please, and the aggregate will be equally easy of expression. When, however, the *apothecaries'* system is followed in the prescription, at once a complication arises, for the reason that in apothecaries' weight all amounts are *not* equally easy of expression—some, indeed, being so awkward to express as practically to be unavailable. Thus, for instance, although by this system, as already pointed out, ratios are naturally taken in duodecimals, yet such a natural duodecimal multiple as *seventy-two*, representing grains, is a monstrosity for expression. In computing, therefore, by apothecaries' weight and measure, the prescriber is bound by the clumsiness of the denomination ratios of the system, and so, for cases in which the total basis exceeds a drachm, finds available for the fulfilment of the tripartite conditioning set forth above, a certain set of combinations only. These combinations the young prescriber must learn by rote. They are easily enough figured out for one's self;

but for convenience of reference there are set forth, in tabular form below, the combinations convenient when the individual dose of basis is to be one or other of the several amounts, *five, ten, fifteen,* or *twenty* grains. If the individual dose of basis be *less* than a grain or two, then the total amount of basis required, being but a *moderate number of grains*, is easy enough of expression, and the difficulty now under consideration does not obtain.

TABLE OF CONVENIENT COMBINATIONS FOR THE PRESCRIPTION OF FLUID MIXTURES BY APOTHECARIES' MEASURE AND WEIGHT.

1. *Dose to be borne in an average teaspoonful, reckoning six teaspoonfuls to the fluidounce.*

Capacity of phial in fluidounces.	Number of teaspoonfuls contained.	Amount of Basis to be Prescribed in order to Yield to the Teaspoonful the several Doses of			
		Five grains.	Ten grains.	Fifteen grains.	Twenty grains.
½	3	gr. xv.	℈ ss.	....	ʒ i.
1	6	℈ ss.	ʒ i.	ʒ iss.	ʒ ij.
2	12	ʒ i.	ʒ ij.	ʒ iij.	℥ ss.
4	24	ʒ ij.	℥ ss.	ʒ vi.	℥ i.
6	36	ʒ iij.	℥ vi.	℥ ix.	℥ iss.
8	48	℥ ss.	℥ i.	ʒ iss.	℥ ij.
12	72	℥ vi.	℥ iss.	.	℥ iij.

2. *Dose to be borne in an average tablespoonful, reckoning one and a half tablespoonfuls to the fluidounce.*

Capacity of phial in fluidounces.	Number of tablespoonfuls contained.	Amount of Basis to be Prescribed in order to Yield to the Tablespoonful the several Doses of—			
		Five grains.	Ten grains.	Fifteen grains.	Twenty grains.
2	3	gr. xv.	℈ ss.	...	ʒ iij.
4	6	℈ ss.	ʒ i.	℈ iss.	ʒ ij.
6	9	...	℈ iss.	.	ʒ iij.
8	12	ʒ i.	ʒ ij.	ʒ ij.	℥ ss.
12	18	℈ iss.	ʒ iij.	....	℥ vi.

3. *Dose to be borne in a measured fluidrachm.*

Capacity of phial in fluidounces.	Number of fluidrachms contained.	Amount of Basis to be Prescribed in order to Yield to the Fluidrachm the several Doses of—			
		Five grains.	Ten grains.	Fifteen grains.	Twenty grains.
½	4	ʒ i.	ʒ ij.	℥ i.	ʒ iv.
1	8	ʒ ij.	ʒ iv.	℥ ij.	ʒ viij.
2	16	ʒ iv.	ʒ viij.	℥ ss.	ʒ xvi.
4	32	ʒ viij.	ʒ xvi.	℥ i.	.
6	48	℥ ss.	℥ i.	℥ iss.	℥ ij.
8	64	ʒ xvi.	.	℥ ij.	.
12	96	℥ i.	℥ ij.	℥ iij.	℥ iv.

4. *Dose to be borne in a measured half-fluidounce.*

Capacity of phial in fluidounces.	Number of half-fluidounces contained.	Amount of Basis to be Prescribed in order to Yield to the Half-Fluidounce the several Doses of			
		Five grains.	Ten grains.	Fifteen grains.	Twenty grains.
1	2	gr. x.	ʒ i.	℈ ss.	ʒ ij.
2	4	ʒ i.	ʒ ij.	℈ i.	ʒ iv.
4	8	ʒ ij.	ʒ iv.	℈ ij.	ʒ viij.
6	12	℈ i.	℈ ij.	℈ iij.	℥ ss.
8	16	ʒ iv.	ʒ viij.	℥ ss.	ʒ xvi.
12	24	℈ ij.	℥ ss.	℈ vi.	℥ i.

III. THE EXPRESSING OF A PRESCRIPTION.—A prescription is an order, *dated* and *signed*, to the pharmacist to take certain quantities of certain several substances; to perform upon them certain pharmaceutical operations; to label the package with certain directions concerning use, and to address it with the name of the patient. Upon this order the author may also have occasion to set down certain injunctions, such as "not to be renewed," or, "not to be shown to the patient," etc. In *form*, prescriptions are commonly written after the following paradigm:

[*Not renewable without authority.*]

For Mr. A. B.

Take
Of substance *A*, quantity *x*.
Of substance *B*, quantity *y*
Of substance *C*, quantity *z* [etc.]
Do so-and-so [with them]. . . . . .
Label [the package] . . . . . .
[*Signed*] C.D., M.D.,
No. 1 Blank Street.

[Dated] November 22d, 1886.

Instead of a written signature, a very common and a very good plan, followed by many practitioners, is to have prescription blanks printed for their personal use, bearing the imprint of name, address, and office hours. In such case the imprint is commonly at the head of the paper. In *language*, a prescription is commonly written in part in Latin, and in part in the vernacular. In the United States the use of the Latin is commonly confined to such portion of the prescription as has to do with directions to the pharmacist for the compounding and "putting up" of the medicine; but in many other countries the *directions for use* are also written in Latin. This latter foreign custom has nothing to commend itself, but, on the contrary, is intrinsically objectionable on the score of opening an unnecessary doorway for the entry of mistakes. For such directions must, of necessity, finally appear in the vernacular in the label upon the package which is to serve for the patient's guidance; so that, to write them in the prescription in Latin is to entail their translation back into the vernacular at the hands of the pharmacist for the purpose of transcription, all at the risk of mistakes. Far better is the American custom, whereby the prescriber can—and always *ought*—set down, in the vernacular, in *full necessary detail*, the directions for administration, which directions are then simply to be copied, *exactly as written*, in the labelling of the package. Another, and quite universal, custom is to express by *abbreviation* or by *symbol*, in the pharmaceutical portion of the prescription, what might be called *staple* words. Thus, in the foregoing paradigm, *take* is expressed by the symbol "℞," which, originally the astronomical sign "♃," of the planet Jupiter (symbolical of the prayer to the deity Jove which in ancient times headed prescriptions), now bears its present peculiar form in order to do duty also as the initial letter of the Latin word *recipe*, signifying *take thou*. Next, titles of denominations of weight or measure are expressed by the commonly employed symbols for such denominations, and numeral adjectives by the so-called *Roman* numerals in the use of the *apothecaries'* system of weight or measure; but by the ordinary *Arabic* numerals when the prescription is by *metric* weight or measure, as is practically a necessity for the expression of the related integral and decimal fractions by which metric quantities are signified. Next, the word *misce*, signifying *mix thou*—the most commonly occurring word expressing requirement of pharmaceutical manipulation, is expressed by its initial letter *M.*, and similarly, and lastly, the word *signa*, signifying *label thou*, by its initial letter *S*. Other commonly employed abbreviations are "āā" for *ana*, latinized Greek for the phrase *of each;* "no." for *numero*, signifying *to the number of;* "q. s." for *quantum sufficiat*, signifying *as much as may be necessary*, and "p. r. n." for *pro re natâ*, signifying *according to need*.

It thus appears that all of the prescription requiring full dress in Latin is comprised in the titles of substances prescribed, and in the directions for the compounding. And for the correct latinizing of such items a critical knowledge of the Latin language, though, of course, of great advantage, is yet not indispensable. For, so far as relates to the expression of *medicine-titles*, all that is necessary is to know how to set these titles in proper *case;*

and, as concerns the expression of *pharmaceutical directions*, it is to be remembered that, in the great majority of instances, the directions for compounding requiring specification in prescription writing, are simple and set, so that their Latin phrasing is easily compassed by the knowledge of a few arbitrary words and phrases. Indeed, for all but seldom occurring exceptional directions, the latinizing can be effected by the words and phrases in the following list, properly coupled with Latin words signifying forms of medicines, presumably already learned.

List of Odd Words and Phrases of Common Occurrence in the Expression of Pharmaceutical Directions, in Prescriptions.—1. *Verbs*, in *imperative mood*; "object" to be in the *accusative* case (analogue of the English *objective*):

Ádde, add.	*Filtra*, filter.
Cóla, strain.	*Mácera*, macerate.
Divide, divide.	*Misce*, mix.
Exténde, spread.	*Sólve*, dissolve.
Fac, make.	*Tére*, rub.

2. *Verbs*, in *subjunctive mood*, taking a *subject* or a *predicate*, *nominative*:

Búlliat, let [it] boil.
Fiat, let [*it*] be made [into].
Fiant, let [*them*] be made [into].

3. *Verbal adjective* (participle) to agree with its noun in gender, number, and case:
Dividéndus (masculine); *-a* (feminine); *-um* (neuter), to be divided.

4. *Prepositions:* noun following to be in the *accusative* case:

Ad, to; up to. *In*, into. *Súpra*, upon.

5 *Prepositions:* noun following to be in the *ablative* case:

Cum, with. *Pro*, for.

6. *Miscellaneous Words and Phrases:*

Ána, of each.	*Guttátim*, by drops.
Béne, well.	*Non*, not.
Bis, twice.	*Sémel*, once.
Dein or *déinde*, thereupon.	*Simul*, together.
Et, and.	*Statim*, at once.
Gradátim, gradually.	*Ter*, thrice.

In the instance of a pharmaceutical operation which cannot be expressed in Latin by the application of the foregoing vocabulary, the wise course, even for the Latin scholar, is to forego elegance and write the direction in the vernacular. Otherwise it might chance that the prescription overstep the pharmacist's capacity for translation, to the obvious defeat of the compounding.

As regards the rendering, in proper Latin case, of the titles of the ingredient substances of a prescription, the points are as follows: There are, in Latin, six cases in the declension of nouns and adjectives, but of these cases four only are concerned in the latinizing of medicine titles. These four are, respectively, as follows: The *nominative* case, corresponding to the English nominative, is the case in which titular words stand in simple statement—by which, in short, names are learned. Thus we recognize prepared chalk by the Latin title *Creta præparata*, wherein the two words of the title are in the nominative case. Next, the *genitive* case corresponds to the English *objective* case after the preposition *of*, and is the case in which titular words most commonly stand in prescription writing. For, in the first place, *compound* titles, even in simple statement, commonly afford an instance of the genitive, as in the case of the title *tincture of opium*. Here the phrase *of opium* is rendered in Latin by the word *opium* set in the genitive case. Then, in the second place, in prescribing, the order for the "taking" of a given ingredient is, in the enormous majority of instances, a direction for the taking of a specified *quantity* of the substance in question. A prescription for a phial of laudanum, that is, will read: "Take *of* tincture of opium one-half fluidounce." In such case the titular word of the preparation itself—in this instance the word *tincture*—will have to stand in the genitive, since now it, also, follows the preposition *of*. With the exception, therefore, of a few conditions when titular words stand, in prescription expression, in the *accusative*, the rule is that all titular nouns and adjectives which, in simple statement of the title, stand in the *nominative*, require, in prescription orders, to be set in the *genitive*.

The third Latin case that concerns the prescriber is the *accusative*, the Latin analogue of the English *objective following a transitive verb*. Titular nouns and adjectives take the accusative under the two following circumstances: First, when the order is not the common one to take a certain specified measure or weight *of* the thing, but to take *the thing itself* in a conditioned entirety. A common instance of this circumstance is where yolk or white of egg is an ingredient of a prescription. Here by the condition of things it is easiest to measure quantity by the natural measure of the egg substance itself. Hence, in prescribing yolk the order is commonly to *take the yolk of one egg*, or of two, or of three eggs, as the case may be; in which case the title word *yolk*, standing as the direct object of the transitive verb *take*, requires to be put in the accusative. Another commonly occurring instance where the accusative must appear, is where the prescriber writes for a certain *number* of a ready-made medicinal *entity*, such as pills or troches, of standard composition, and hence of independent title. Thus, to prescribe the pharmacopœial *compound cathartic pill*, the simplest way is to order directly the desired *number* of the already made pills, which the pharmacist keeps in stock. Such prescription, therefore, reads: "Take compound cathartic pills to the number of" so many, and so the word for *pills*, with its dependent adjectives, appearing as the immediate object of the verb *take*, stands in the accusative. The second circumstance determining the setting in the accusative of titular nouns and adjectives occurs, in one form of writing, in cases in which the prescription orders that a given substance be taken *up to the attainment of a certain total bulk or weight*. This form of order most commonly obtains in the prescription of fluid mixtures, where it is often convenient to order in specified quantities the necessary amounts, respectively, of basis or adjuvant; but, as regards the inert *vehicle* simply to direct the compounder to "take" the vehicle substance until the whole mixture shall attain the measure of the desired bottleful. In such case the order for the vehicle may be phrased in either of two styles—in the one of which the titular words will appear as usual in the genitive, but, in the other, in the accusative. The phrase in the latter style is according to the model, *take so-and-so up to* [*the measure of*] *so much*. Here the title of the substance "taken" is the immediate object of the verb *take*, and therefore stands in the accusative; the phrase *up to the measure of* being expressed by the preposition *ad*. The other style of phrasing the order is after this model: *Take of so-and-so as much as may be necessary to attain the measure of so much*. Here the title of the medicine once more follows the preposition *of*, and hence appears in the genitive. In the rendering of the order in this style, the Latin phrase *quantum sufficiat ad* (commonly abbreviated to *q. s. ad*) is the translation of the English "as much as may be necessary to attain the measure of."

The fourth and last Latin case that concerns the prescriber is the *ablative*, a case corresponding to the English objective after certain prepositions. The prepositions governing the ablative that occur in prescription writing are *cum*, "with," and *pro*, "for." The former of these occurs in a few titles, as for instance, *Hydrargyrum cum Cretâ*, mercury with chalk; *Emplastrum Picis cum Cantharide*, pitch plaster with cantharides; and the latter in the much-used phrase *pro re natâ*, "according to need." But as regards the ablative, the special point obtains that the circumstances of prescription phrasing never require the rendering in the ablative of a title word which in the title appears in a different case. The few instances of

the ablative in medicine titles are therefore fixed, and the ablatives so occurring are easily learned by rote.

The *expression* of case is, in Latin, effected by modification of the ending of the word itself which is to be declined, and in such modification, *adjectives* share as well as nouns. Different modifications are employed to signify case in the singular and plural number, respectively, and of such modifications there are, in ordinary, five distinct systems, constituting the five several *declensions* of nouns and adjectives, besides cases of irregular declension presented by certain pronouns and cardinal numerals. Of the five systematic declensions, one, the *fifth*, affords but a single example in prescription Latin, namely, the ablative *re* of the noun *res* in the oft-quoted phrase *pro re natâ*. Of the other four declensions, examples occur in prescription-writing of the *nominative, genitive, accusative,* and *ablative* cases, respectively, in the singular number, and of the *nominative, genitive,* and *accusative* in the plural. The following table shows the endings for the several cases so enumerated, so far as concerns nouns and adjectives embraced in the prescriber's vocabulary. Endings for nouns not in such vocabulary are purposely omitted, as are also the irregular declensions of pronouns. In the table the italicized letters *m.*, *f.*, and *n.*, signify respectively, that the case endings in the columns beneath are those of nouns or adjectives of the *masculine, feminine,* or *neuter* gender; for, as appears in the table, case endings often differ, even in the same declension, according to the gender of the word. The endings of the first and second declensions, severally, which appear *in parenthesis*, are the endings of certain Greek nouns, adopted into Latin with something of the Greek form retained. The table also gives a list of words of foreign origin applied as drug titles, which, following the Latin idiom in such case, make no change of ending to signify case—are, in short, *indeclinable*.

TABLE OF PARTS OF LATIN DECLENSIONS SO FAR AS EXEMPLIFIED BY WORDS USED IN PRESCRIPTION-WRITING.

1. *Regular Declensions of Nouns and Adjectives.*

	First declension.	Second declension.		Third declension.		Fourth declension.
		*m.**	*n.*	*m.* and *f.*	*n.*	*m.*†
SINGULAR.						
Nominative	-a (-e)	-us (-os)	-um (-on)	(various)	various)	-us
Genitive ...	-æ (-es)	-i		-is		-us
Accusative .	-am (-en)	-um (-on)		-em	(like nom.)	-um
Ablative ...	-â	-o		-e		
PLURAL.						
Nominative	-æ	-i	-a	-es	-a	-us
Genitive ...	-arum	-orum		-um,	-ium	-uum
Accusative .	-as	-os	-a	-es	-a	-us

(Fifth Declension exemplified only in ablative singular *re* in phrase *pro re natâ*.)

* Except *juniperus, prunus, rhamnus, sambucus,* and *ulmus*, feminine.

† Except *quercus*, feminine.

2. *Declension of Cardinal Numerals.*

	Unus, One.			*Duo*, Two.			*Tres*, Three.	
	m.	*f.*	*n.*	*m.*	*f.*	*n.*	*m. and f.*	*n.*
Nominative	un-us	-a	-um	du-o	-æ	-o	tr-es	-ia
Genitive ...	-ius			-orum	-arum	-orum	-ium	
Accusative .	-um	-am	-um	-os	-as	-o	-es	-ia

All other cardinal numerals are indeclinable.

INDECLINABLE DRUG-TITLES—*all neuter.*

Alcohol,	Catechu,	Eucalyptol,
Amyl,	Chloral,	Kamala,
Buchu,	Cusso,	Kino,
Cajuputi,	Elixir,	Matico,

INDECLINABLE DRUG-TITLES *all neuter. Continued.*

Menthol,	Pyrogallol,	Sumbul,
Methyl,	Salol,	Thymol.
Naphtol,	Sassafras,	

As appears at a glance from the foregoing table, in the case of any noun or adjective belonging to either of the three declensions numbered as *first, second,* and *fourth*, respectively, if the *nominative* be given, any other case can at once be formed by substituting the proper case ending for that of the nominative. In words of the *third* declension, however, this possibility in very many cases does not obtain. For in this declension the *nominative* often stands apart from the other cases in the way of having the very root, or "stem," of the word curtailed or modified in its construction. Thus, the stem *anthemid-*, giving genitive *anthemidis*, accusative *anthemidem*, and ablative *anthemide*, gives nominative *anthemis*—a word in which the full stem does not appear. Similarly, the root *flor-*, giving genitive *floris*, etc., gives nominative *flos;* and root *rho-*, giving genitive *rhois*, offers the much modified nominative form *rhus*. Hence, for the proper rendering in oblique case of nouns or adjectives of the *third* declension, it becomes necessary to learn arbitrarily the form of some one of the oblique cases—most conveniently the genitive—as well as that of the nominative.

A special point concerned in the expression of case obtains in the case of *adjectives*, to the effect that very many of these words form their case endings after different ones of the declension models, according to the *gender* of the noun to which the adjective is attached. In compound drug titles, therefore, which include an adjective, the gender of the noun modified by the adjective becomes necessary to know for the *intelligent*, proper rendering of the adjective's case ending. Of course, such knowledge is not essential, since the title, adjective, and all, can be learned by rote, and then, remembering the nominative form of the adjective, the necessary change to genitive or accusative, to suit the requirement of the prescription phrase, can be done by rule. But it saves a vast amount of unnecessary memorizing to understand the system, so far as system goes, by which genders of Latin nouns are determined. Reverting, then, to the above declension table, it appears that all prescription occurring nouns of the *first* declension are *feminine* in gender; all those of the *second* declension ending in *-um*, or *-on*, are neuter, and, with a few exceptions, all of the *second* declension ending in *-us*, or *-os*, and all of the *fourth* declension ending in *-us*, are *masculine*. The exceptions in the two latter instances are nouns in *-us*, representing ancient Latin *tree-names*, which, because of the ancient Latin conception of an inherent femininity in trees as things, take the feminine gender in spite of their etymologically masculine nominative ending. In the *third* declension all genders appear, and, although in nouns of certain nominative endings the ending carries with it the gender, yet in the case of many other nouns this is not so, and genders must be learned arbitrarily. Happily, however, the number of nouns of the third declension, among drug titles, which bear an associated adjective, are quite few.

From the above analysis it is evident that, in the case of a given *noun* in the nominative, the rendering of the same in an oblique case can proceed by rule according to the foregoing declension table, if only the declension of the noun be known; with the further item, in the instance of a noun of the *third* declension, that some one oblique case, as well as the nominative, be known, for the affording of the full stem of the word. Similarly, the proper case dress of any given *adjective* can be fixed if the scheme of declension of the adjective itself be known, on the one hand, and, on the other, the gender of the noun to which the adjective is to be affixed—adjectives requiring to agree with their respective nouns in gender, number, and case. This requisite information concerning nouns and adjectives of prescription use is afforded in the two following tables—the one giving a key to the declensions of nouns, with genders, and also, in the case of nouns of the third declension, genitive end-

ings—and the other showing the schemes of declension of adjectives.

TABLE SHOWING DECLENSION AND GENDER OF NOUNS OCCURRING IN TITLES OF U. S. PHARMACOPŒIAL MEDICINES AND IN COMMON PRESCRIPTION TERMS.

Nominative singular ending in **-a:**

All First Declension and Feminine, except of Greek origin the following in *-ma*:

Physostig'ma (physostig'matis), *3d, n.*
Aspidosper'ma (aspidosper'matis), *3d, n.*
Enema (ene'matis), *3d, n.*
Catapla'sma (catapla'smatis), *3d, n.*
Gargari'sma (gargari'smatis), *3d, n.*
Theobro'ma (theobro'matis), *3d, n.*

Nominative Singular ending in **-us:**

All Second Declension, Masculine, except–

Juni'perus, *2d, f.*
Pru'nus, "
Rha'mnus, "
Sambu'cus, "
U'lmus, "
Rhus (rho'is), *3d, f.*
"Prunus glabra".
Fru'ctus, *4th, m.*
Spi'ritus, "
Que'rcus, "

Nominative Singular ending in **-os:**

Comprise only the following

Flos (flo'ris), *3d, m.*
Bos (bo'vis), *3d, m.* or *f.*

Nominative Singular ending in **-um:**

All Second Declension, Neuter.

Nominative Singular ending in **-on:**

Comprise only the following–

Eriodi'ctyon, *2d, n.*
Hæmato'xylon, "
Toxicode'ndron, "
Eri'geron (erigero'ntis), *3d, n.*
Li'men (limi'nis), *3d, m.*

Nouns of all other endings are of Third Declension, and are as follows:

Ending in **-e:**

Lac'ca (lac'cis), *n.*

Ending in **-el:**

Fel (fe'llis), *n.*
Mel (me'llis), *n.*

Ending in **-en:**

Alu'men (alu'minis), *n.*
Se'men (se'minis), *n.*

Ending in **-o:**

(*-io*)
Confe'ctio (confectio'nis), *f.*
Lo'tio (lotio'nis), *f.*
Po'rtio (portio'nis), *f.*
Tritura'tio (trituratio'nis), *f.*
(*-go*)
Mucila'go (mucilagi'nis), *f.*
(*-bo* and *-po*)
Ca'rbo (carbo'nis), *m.*
Pe'po (pepo'nis), *m.*
Sa'po (sapo'nis), *m.*

Ending in **-r:**

(*-er*)
Æ'ther (æ'theris), *m.*
Pi'per (pi'peris), *n.*
Zi'ngiber (zingi'beris), *n.*
(*-or*)
Li'quor (li'quoris), *m.*
(*-ur*)
Su'lphur (su'lphuris), *n.*

Ending in **-s:**

(*-as*, genitive *-atis*)
Ace'tas (aceta'tis), *m.*
[*and all salt-names in -as.*]

(*-as*, genitive *-adis*)
Ascle'pias (asclepi'adis), *f.*

(*-is*, genitive *-idis*)
Arsenis (arseni'tis), *m.*
[*and all salt-names in -is.*]

(*-is*, genitive *-idis*)
A'nthemis (anthe'midis), *f.*
Ca'ntharis (cantha'ridis), *f.*
Colocy'nthis (colocy'nthidis), *f.*
Hamame'lis (hamame'lidis), *f.*
I'ris (i'ridis), *f.*
Ma'cis (ma'cidis), *f.*

(*-is*, genitive *-eris*)
Pu'lvis (pu'lveris), *m.*

(*-is*, genitive *-is*)
Ca'nnabis (ca'nnabis), *f.*
Digita'lis (digita'lis), *f.*
Hydra'stis (hydra'stis), *f.*
Sina'pis (sina'pis), *f.*

(*-os, see ante.*)

(*-us, see ante.*)

(*-ns*)
Juglans (jugla'ndis), *f.*

(*-ps*)
A'deps (a'dipis), *m.*

(*-rs*)
Pars (pa'rtis), *f.*

Ending in **-x:**

(*-ax*)
Bo'rax (bora'cis), *m.*
Sty'rax (styra'cis), *m.*

(*-ex*)
Co'rtex (co'rticis), *m.* and *f.*
Ru'mex (ru'micis), *f.*

(*-ix*)
Pix (pi'cis), *f.*
Ra'dix (radi'cis), *f.*

(*-ux*)
Nux (nu'cis), *f.*,

(*-lx*)
Calx (ca'lcis), *f.*

TABLE SHOWING SCHEMES OF DECLENSION AND GENDER OF ADJECTIVES OCCURRING IN U. S. PHARMACOPŒIAL MEDICINAL TITLES AND IN PRESCRIPTION-PHRASES.

SCHEME I.—*Second and First Declensions Combined.*

Masculine.	*Feminine.*	*Neuter.*
-us [2d dec.]	*-a* [1st dec.]	*-um* [2d dec.]

SCHEME II.—*Third Declension.*

Masculine and Feminine.	*Neuter.*
-is (genitive *-is*).	*-e* (genitive *-is*).

SCHEME III.—*Third Declension.*

Masculine and Feminine.

-or (genitive *-oris*).

SCHEME IV.—*Third Declension.*

All Genders.

-ens (genitive singular *-entis*; genitive plural *-entium*).

In commentary upon the declension schemes of adjectives set forth in the foregoing table, it may be stated that Scheme I. embraces by far the greater number of adjectives. In this scheme the neuter ending *-on*, borrowed from the Greek like the same ending among nouns of the second declension, finds among drug titles but a single example, *diachylon*. Scheme II. embraces a few adjectives only among those occurring in medicine titles, and affords an example of the nominative ending *-e* of the third declension, which does not occur among *nouns* of pharmacopœial titles. Scheme III. offers a single example only, viz., *fortior*. Of Scheme IV. pharmacopœial adjectives give but two examples, namely, *effervescens* and *recens*. A survey of the *genders* marked on the table shows that in every case a distinctive gender, where there is such, can be told from the adjective nominative ending.

A final point, concerning the expression of a prescription, is that, having regard to the fact that a *slip of the pen* on the part of the writer, or a *slip of the understanding* on the part of the pharmacist reader of a prescription, may convert what was meant as a missive of mercy into a death warrant, it behooves the prescriber most solemnly to execute his task *deliberately, thoughtfully*, and, in chirography, *legibly, abjuring all dangerous cloak-of-ignorance abbreviation of medicine-titles;* and, finally, to fail not of that trusty safeguard against error, a *review of the paper* after the writing. *Edward Curtis.*

PROTOZOA.—Standing distinctly as the lowest of all animal organisms, the protozoa constitute a branch differentiated from higher groups by the simplicity of organization in that the animal consists of but a single cell or a colony of simple cells. In the main the animals of this group are easily recognized, although some forms are so generalized, and partake of plant characteristics to such an extent as to render their classification doubtful; and, on the other hand, certain higher forms show the first stages in specialization among cells of the colony which ultimately leads to the differentiation of the metazoan organism.

The Protozoa are true cells and possess consequently neither organs nor tissues. In the discharge of all living functions by the single cell, however, one finds a physiologic complexity as striking as the morphologic simplicity. The latter is also less extreme in many cases where specialization has effected the production of individual features within the single cell, differentiations which subserve particular functions, and which are thus analogous to the organs of the metazoa. Such are denominated cell organs, or organellæ, and are of great variety. Among these may be mentioned the locomotor structures, such as pseudopodia, flagella, and cilia, the numerous vacuoles of a nutritive and contractile type, the preformed, often highly modified openings for ingestion of food and egestion of solid waste matter, and various protective coverings of a permanent character or temporary and connected with reproduction.

As true cells all Protozoa possess one or more nuclei, and the earlier contention that there exists a special group of anuclear organisms, the monera of Haeckel, has not been confirmed by later study. The simple protozoon is with a single known exception (*Loxodes rostrum*) uninuclear, and the presence of many nuclei points to a colonial organism or to a reproductive phase, except that in one large group two forms of nuclei coexist and divide the functions otherwise resident in the single nucleus.

The reproduction of the Protozoa is again that of the

cell, viz., by division, which may be simple or multiple, and in varied form, either while free or in the encysted condition. Two types of division may alternate regularly or indefinitely in the life cycle of a given species, and in most subdivisions of the group certain so-called sexual processes have been demonstrated. These consist in general in the fusion of similar individuals (isogametes), or of dissimilar (macro- and microgametes), or merely in the mutual exchange of nuclear matter.

In regard to location parasitism among the Protozoa affords conditions not found otherwise. There are in this group not only organ parasites, as in the groups of helminthes, but also such forms as must be designated tissue parasites, cell parasites, and even nuclear parasites. Different phases in the life cycle of the same species may illustrate different modes of parasitism, as is the case with the malarial organisms, which at various epochs in the life history are successively cell parasites in the erythrocytes, organ parasites in the blood-vessels, and tissue parasites in the wall of the mosquito's midgut.

In general, however, the protozoan parasites repeat conditions already described for Metazoa. One finds the degeneration of organs superfluous under conditions of parasitic existence, the formation of organs of attachment, such as hooks, suckers, etc., the noteworthy fecundity already commented upon for metazoan parasites; and finally the alternation of generations and of hosts is a common feature among the Protozoa also.

An encysted condition of the entire individual or of a group of spores aids in the dispersal of the species, which are all inhabitants of a moist environment and cease activity at once on withdrawal of the water. This general habit renders it difficult to distinguish between mere commensals which find in the alimentary canal of higher forms conditions for their ordinary slime-inhabiting existence without exerting any influence upon the host, and such as are parasites in the true sense.

A true parasite draws its nourishment from the host and affects it at least to that extent. When this takes place, as with protozoan parasites largely, within a tissue or even a cell, morbid conditions are evoked, even though they remain local in some cases. That functional disturbances result is evinced by the relatively large number of protozoan diseases among animals and plants. These sometimes take the form of tissue proliferations, as has been clearly demonstrated for plants. An effort to trace similar effects in animals is found in the extensive literature on cancer parasites. Thus far, however, no sufficient evidence has been brought to establish the parasitic nature of such abnormal growths, and none of the supposed "parasites" can be clearly recognized as Protozoa. It should be noted in passing that in addition to the mechanical effect of cell parasites a chemical influence of at least equal importance is exercised by the excretions of the organism, the metabolic products set free in the protoplasm of the host cell. In some cases this is a factor of great importance, as also in the case of bacterial diseases; its significance among Protozoa is not yet sufficiently investigated.

It is noteworthy that in many instances a protozoan infection is self-terminating, either that a type of immunity is acquired by the host, or that the reproductive cycle of the parasite reaches its limit without a change of host or alternation of generations. MacNeal and Novy have recently endeavored to determine experimentally the possibility of securing attenuated cultures of one protozoan parasite (*Trypanosoma*) with absolutely negative results; the last generation from a culture more than a year old was even more virulent than the organism at the start.

Regarding means of infection but little definite evidence is at hand. It is inferred that encysted forms furnish the ordinary means for transferring the species to a new host, and yet in many cases experiments along this line have been without results. In other cases it is now known that the transfer takes place through some biting insect, which in some cases, if not all, acts as the host for another phase in the life history of the parasite, and is capable of transmitting the disease only after a period sufficient to allow of the development within its body of the specified portion of the life cycle.

In those cases in which the life history has been worked out, means of preventing the infection of the human host constitute the evident limitation to the spread of the disease caused by the parasite. The inauguration of a simple but effective prophylaxis for malaria and yellow fever ranks rightly as among the most brilliant achievements of scientific medicine. In cases in which the life history of the parasite is unknown, the prophylaxis is necessarily vague and uncertain. It is wise to emphasize here the importance of co-operative effort on the part of trained observers, both in medicine and in zoology, to elucidate fully the problems which necessarily offer almost insuperable obstacles to the investigator approaching them from the single standpoint.

All the varied modifications within the branch of Protozoa may be grouped into four well-defined classes which are now almost universally recognized. These may be briefly outlined together with their major subdivisions, following in the main the classifications of Bütschli, Calkins, and Doflein, and noting principally those groups which contain forms found in the human body.

Class I. Sarcodina.—Naked or shelled Protozoa, characterized in the free adult condition by the formation of changeable processes of protoplasm as organs of locomotion. These pseudopodia may be lobose, digitate, reticulate, or finely radiate, and may be formed over the entire surface of the body, or only at definite points. Reproduction takes place by simple division and by spore formation.

Subclass 1. Rhizopoda. Naked or shelled Sarcodina, having lobose or reticulate pseudopodia. The young may be flagellate as well as amœboid, and are produced by multiple division of the active cell or during encystment. Included among Amœbina are naked forms (Gymnamœbina) with both free and parasitic species, and also shelled forms (Thecamœbina) only free living.

Subclass 2. Heliozoa. Naked or shelled Sarcodina, typically spherical, with little change of form by amœboid movements. Pseudopodia fine, filiform, radiating from all parts, provided with axial filament and rarely changeable, exclusively free living forms.

Subclass 3. Radiolaria. Marine Sarcodina with pseudopodia like those of Heliozoa, but always provided with internal chitinous capsule which encloses the nuclei. Skeleton of acanthin or silica sometimes absent. A very large group of free living forms.

Subclass 4. Mycetozoa. Terrestrial saprophytic or parasitic forms, also known as Myxomycetes or slime moulds, and included under the fungi by some botanists. The motile amœboid or flagellate swarm spores, the plasmodia or colonies formed by the fusion of numerous amœboid individuals, and the holozoic mode of nutrition are characteristically animal features. On the other hand, the production of spores in sporangia, often provided with stalks and other plant-like structures, are taken to prove the plant nature of these forms. All known parasitic forms in this group attack plants.

Class II. Mastigophora.—Protozoa of variable form, naked or with cell membrane; they move by flagella, which vary in number from one to eight on each cell.* Mouth, contractile vacuole, and definitely formed nucleus usually present. Small forms with tendency to formation of colonies.

Subclass 1. Flagellata. Small organisms with one or more flagella at anterior end, usually actively motile, but capable of encystment. Reproduction by longitudinal fission of free form or by multiple division in encysted stage. Rarely transverse fission occurs.

Subclass 2. Dinoflagellata. Naked or shelled forms with two flagella, one of which extends out from the body, while the other is wrapped around the animal. No parasitic forms.

* *Multicilia lacustris* Cienkowsky has many flagella, distributed over the whole body.

Subclass 3. Cystoflagellata. Large marine forms with parenchymatous protoplasm and firm membrane; marine; no parasitic forms.

Class. III. Sporozoa.—Exclusively parasitic forms, in the adult condition without flagella or cilia, contractile vacuole, and opening for ingestion of solid food. Reproduction always by spore formation, usually within a firm membrane. Alternation of generations only exceptionally wanting. The young forms regularly begin the life cycle as cell parasites; other stages may be the same, or tissue or organ parasites.

Subclass I. Telosporidia.—At the end of a vegetative period the entire cell divides into sporocysts.

Order 1. Gregarinida. Vegetative stage intracellular at first, full-grown organism extracellular; fertilization isogamous, fertilized forms permanently extracellular. A large group of forms parasitic in alimentary and body cavities of invertebrates.

Order 2. Coccidiomorpha. Vegetative stage permanently intracellular; fertilization anisogamous; sexual generation permanently or temporarily intracellular. Many of the most important protozoan parasites of man fall in the limits of this group.

Subclass 2. Neosporidia.—Sporocysts are produced continually and at the expense of only part of the cell. In general these forms are not well known.

Order 1. Cnidosporidia. The spores possess one or more polar capsules which contain a coiled thread like a nematocyst. The sub-orders are: (1) Myxosporidia, parasitic in water-inhabiting vertebrates; and (2) microsporidia in certain invertebrates also. Both are not important here.

Order 2. Sarcosporidia. Parasitic in muscle cells of terrestrial vertebrates, probably without polar capsule. Little known, but important.

Class IV. Infusoria.—Protozoa with motor organs in the form of cilia, whether simple or united into membranes, membranellæ, or cirri; with macro- and micronucleus; reproduction by division and by budding, combined with an exchange of nuclear matter known as conjugation.

Subclass 1. Ciliata. Cilia persistent except when encysted. Cytostome usually present. Mostly free forms; some parasites of man and other animals.

Subclass 2. Suctoria. Cilia only on young swarming stage. Food taken in by special sucking tubes; no cytostome. No human parasites.

According to this classification the forms which have been reported from man may be arranged as given in the following list, in which, however, chiefly those species are included which are definitely accepted. Some few doubtful forms of special significance are listed here; and still others are referred to in the text under general headings.

Class Sarcodina.
- Subclass Rhizopoda.
  - Order Amœbina.
    - Suborder Gymnamœbina.
      - Entamœba coli.
      - Entamœba histolytica.
      - Amœba Miurai.
      - Leydenia gemmipara.

Class Mastigophora.
- Subclass Flagellata.
  - Order Protomonadina.
    - Cercomonas hominis.
    - Monas pyophila.
    - Trypanosoma gambiense.
    - Cystomonas urinaria.
  - Order Polymastigina.
    - Trichomonas vaginalis.
    - Trichomonas intestinalis.
    - Lamblia duodenalis.

Class Sporozoa.
- Subclass Telosporidia.
  - Order Coccidiomorpha.
    - Suborder Coccidia.
      - Eimeria Stiedæ.
      - Eimeria hominis.
      - Eimeria bigemina.
    - Suborder Hæmosporidia.
      - Plasmodium malariæ.
      - Plasmodium vivax.
      - Plasmodium immaculatum.
- Subclass Neosporidia.
  - Order Sarcosporidia.
    - Sarcocystis Lindemanni.

Class Infusoria.
- Subclass Ciliata.
  - Order Holotricha.
    - Chilodon dentatus.
  - Order Heterotricha.
    - Nyctotherus faba.
    - Balantidium coli.
    - Balantidium minutum.

The relation of the Protozoa to disease is only just beginning to be investigated. At every point the student is met by the gross insufficiency of present knowledge; a host of isolated observations is on record. Some are clearly wrong, while others are indicative of important discoveries, though the presence of certain organisms during specific diseases needs confirmation, and equally their relation to the inception and progress of the malady. New methods must be worked out for the culture no less than the study of these forms, and the same sort of rigorous analysis is demanded in demonstrating their relation to disease which has been given to bacteria. It seems altogether probable that they will play a prominent rôle in medical investigation in the near future, but in the present state of our knowledge any review of the group must necessarily be only a tentative one.

The class of Sarcodina, or sarcode animals, is typically represented by the common free-living amœba, which has its parallel in the white blood cells. The most characteristic structural feature is the ability to protrude a portion of the body substance in the form of a process or pseudopodium by which locomotion is achieved, and also the food particles are seized and engulfed. The subdivision of the class rests primarily upon the precise character of the pseudopodia.

Under the order Amœbina are included such forms as possess lobose pseudopodia, and the sub-order of Gymnamœbina embraces such of these as are without a shell. All the human parasites which fall within the Sarcodina are included in a few closely related genera of this suborder. While the structure is simple, and in agreement with that of the simple free-living forms of the group, it is impossible to demonstrate that this is not the result of degeneration from more highly differentiated forms by virtue of the parasitic mode of existence. The parasitic species are most probably to be traced back to slime-inhabiting, free-living forms, a transition from which to the present parasitic existence seems most immediate and simple in physiological adjustment.

The ordinary method of reproduction is by simple division, recurring at frequent intervals and conserving the rapid multiplication of the species. This form has long been known, and is to be observed frequently in all truly independent organisms of this type. Recent investigations have disclosed another reproductive type: under definite circumstances, possibly only after fusion of individuals or some exchange of nuclear matter, the amœba forms a cyst within which the nucleus undergoes multiple division, and ultimately the protoplasm arranges itself about the new nuclei, so as to give rise to an equal number of small amœbæ. When these desert the cyst there is left behind a residual mass of protoplasm. At first distinguishable slightly in structure as well as size, the small amœbæ thus produced soon grow to the size and appearance of the adult. The occurrence of this stage in the life cycle has not yet been demonstrated for parasitic amœbæ, except very recently for *Entamœba coli* and *E. histolytica*; but if present it may well be related to the spread of the species as found in the change of hosts. The necessity for such a stage would explain the ineffectual attempts which have been made to inoculate new

hosts by direct transference of the ordinary parasitic form.

In the genus *Amœba* the separation of species is exceedingly difficult on account of the insignificant features available for purposes of differentiation. There are those who lump the forms found in man with such as occur in other mammals under a single species, and there are also those who contend that each host shelters a distinct parasitic species, and bring as evidence the individuality of parasitism in other groups. But on the other hand it may be urged that the amœbæ are not highly differentiated as parasites, and mere difference in host animal has long since been abandoned as a distinguishing mark between parasites from higher classes. It is certain that no positive statement can be made until more complete information is obtained regarding the life cycle of the species. At present no one can affirm that a given species does not possess a free-living generation as well, or even that it is not a normal free-living form which under favorable circumstances has taken up the parasitic mode of life; in which case it should be regarded as a mere accidental parasite. Furthermore of only one human parasite included within this group can it be said positively that it is more than a harmless commensal. Although facts have been adduced to show that others also play a pathogenic rôle, the question must still be regarded as at least an open one.

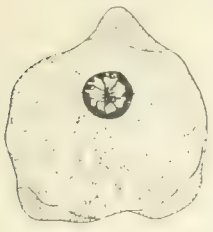


Fig. 5163. "*Amœba coli*," Stained Preparation. Magnified. (After Doflein.)

Among the amœboid bodies which one finds in nature and in cultures many are only developmental stages rather than independent organisms, and the same may well be true of some of the parasitic forms. On the other hand, the distinction between such organisms and various structural elements of the human body is often a very difficult task, and some of the purported parasitic species are in fact referable to the misinterpretation of the body cells referred to above.

In the new genus *Entamœba* are included two important human parasites, the life history of which has recently been well elucidated. The other imperfectly known species are left in the old collective genus *Amœba*, but fuller knowledge may result in the transfer of some or all to this same or other new genera according to the facts ascertained regarding the life history of the individual forms.

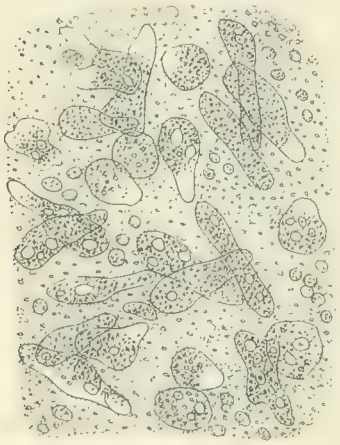


Fig. 5164. "*Amœba coli*," in Intestinal Mucus. Magnified. (From Braun, after Lösch.)*

Entamœba coli (Lösch 1875).—(Syn.: *Amœba coli* Lösch 1875; [?] *Amœba dysenteriæ* Councilman and Lafleur 1891; *Entamœba hominis* Casagrandi e Barbagallo 1897; *Entamœba coli* Schaudinn 1903.)

Form oval or pyriform (Fig. 5163); diameter from 0.0075 to 0.05 mm.; nucleus distinct in life, spherical, 0.002, usually 0.003–0.007 mm. in diameter, with heavy nuclear membrane and many small nucleoli. Ectosarc not distinct save in pseudopodia, where it is conspicuous, everywhere less refractive than endoplasm. Pseudopodia rare, usually one or two, broadly lobed and heavy (Fig. 5164). Endosarc finely granular, with one or several non-contractile vacuoles, and many objects ingested as food; such are leucocytes, erythrocytes, eosinophilia, bacteria, starch granules, fæcal particles, epithelial cells, etc. (Fig. 5165). The digestion of erythrocytes is accomplished without excretion of any pigment masses.

Reproduction in the human intestine by simple division and by schizogony, with the formation normally of eight daughter cells. In fission the nucleus undergoes amitotic division, while in schizogony complicated nuclear changes are seen with the elimination of a portion of the chromatic substance. As a preliminary step to encystment all foreign bodies are extruded from the protoplasm, which thus becomes clear and transparent. These cysts, first discovered by Grassi, were carefully studied by Casagrandi and Barbagallo. They constitute the means of transmitting infection, as has been determined experimentally, first by Calandruccio who swallowed such encysted forms and found the developed amœbæ twelve days later in the fæces. The normal seat of this species is the upper region of the colon, and the vegetative forms appear in the fæces only when the latter are semi-fluid by

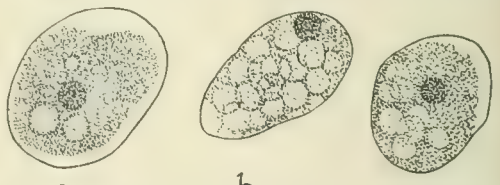


Fig. 5165. "*Amœba coli*," from Dysenteric Intestine, more or less filled with Erythrocytes; Nucleus also visible. Magnified. (From Doflein after Roemer.)*

reason of disease or of the administration of medicaments. The cysts which are so characteristic as to be confused with nothing in the fæces are capable of further development only when they contain eight nuclei. Other cysts have been determined experimentally by Schaudinn to be incapable of development, even though they actually constitute the major part (eighty per cent.) of those evacuated. In old dry fæcal matter only the forms with eight nuclei are present, and in the colon of the next host eight small amœbæ are formed by division of the protoplasm and emerge to begin a new infection and a new vegetative period.

This species occurred in East Prussia in fifty per cent. of the cases examined; in Berlin the number found infected was 1:5, and on the Adriatic coast 2:3. The exact distribution of this species has not been further worked out, though the numerous reports lead one to believe that it is a cosmopolitan species.

Grassi was the first to identify the species from the normal human canal, and Schuberg confirmed this by a considerable series of cases. Casagrandi and Barbagallo demonstrated conclusively that it does not possess pathological characteristics, and quite recently Schaudinn in an exceedingly extensive and careful investigation showed the existence of two very similar species, hitherto generally confused, one of which, that under consideration, is a harmless commensal, and the other to be considered next a dangerous parasite. The first lives in the human host in health and is widely distributed; it multiplies excessively in various intestinal disturbances, and is brought to the exterior in fæcal matter by any conditions which produce fluid or semifluid discharges from the canal. It can indeed coexist with the following species, which is pathological in the extreme. The present

* In advance of the appearance of Schaudinn's figures it did not seem advisable to do more than quote the name given in the original from which these cuts were taken.

species was first carefully studied by Casagrandi and Barbagallo, and is easily recognized from their account. In the majority of cases reported, however, it is difficult to say which form was under examination, although it is probable that in many of them both species were studied and the description contains features characteristic of both. This is the case with the full and valuable account given in Vol. I. of the HANDBOOK. (See *Amœba coli*.) To this admirable review of the subject have been added here only such features as aid in distinguishing the two recently differentiated species.

Entamœba histolytica Schaudinn 1903. (Syn. *Amœba dysenteriæ* Councilman and Lafleur 1891.)

In many general features like *E. coli*, often occurring together with the latter, and heretofore generally confused with it, yet distinguishable by the following features: Ectoplasm well developed and present as distinct plasma zone, more highly refractive than the endoplasm, viscous in consistence and glass-like in appearance. Nucleus rarely visible in life, almost homogeneous; little refractive, poor in chromatin, usually with a single nucleolus in centre, and with very delicate nuclear membrane, if indeed any is present. Reproduction by division and budding, the latter often multiple, and both following amitotic nuclear division. Cysts with eight daughter cells never found. Resting stages are formed when the fæces grow firmer; the progress of their formation begins by the rejection of chromatin from the nucleus until the entire plasma is filled with chromatin masses, and the nucleus itself degenerates and is absorbed or thrown out. The chromatin masses collect in the peripheral zone of the plasma and come to lie in ectoplasmic hillocks, which develop to free spherules on the surface of the cell. These structures measure only 0.003–0.007 mm. in diameter, and soon acquire a yellowish-brown membrane and a highly refractive semi-opaque appearance. The remainder of the amœba goes to pieces. Schaudinn was able experimentally to evoke a severe dysentery by feeding these spores to cats, and maintains on good grounds that such spores constitute the only means of producing a new infection normally. Injections per anum of the vegetative form alone produced a typical case of the disease, as Jürgens showed first.

While *E. coli* has no power to penetrate the healthy epithelium, *E. histolytica* is able to enter anywhere and force its way through. In this process the amœbæ push the cells apart, and even force them free from the layer. These features were first correctly described by Jürgens, who gave a full and accurate account of this species. His discoveries on the cat have been confirmed by the observations of Schaudinn on man also. The amœbæ were found in sound regions of the mucosa in the glands of Lieberkühn, could be followed on into the submucosa. Undermining of the mucosa and abscess formation follows in later stages of the malady. These investigations demonstrate clearly that *E. histolytica* is a true tissue parasite, like the Myxosporidia, and indeed the most dangerous of all Protozoa yet known, and that it is the cause of ulcerous amœbic enteritis.

Jürgens is the only author who in the opinion of Schaudinn has characterized this species in recognizable form, although the species was probably before many authors, who were unable to differentiate it clearly from the other species, *E. coli*, with which it was certainly associated in some cases reported.

The material from which the pathological species was obtained by Schaudinn came from a limited number of cases of tropical dysentery acquired in Egypt, China, and Siam. The real geographical distribution of the species is thus evidently but imperfectly known.

It is difficult to pass satisfactorily upon the specific character of the forms hitherto observed in the United States, and only two references will be made. The observations of Craig (*Medical News*, March 16th, 1901) seem to have been made on *Entamœba coli* of Schaudinn, in which the former described as "oval spots" the formation of the encysted daughter cells already well known from the work of Casagrandi e Barbagallo. The splendid monograph of Councilman and Lafleur in my opinion deals unmistakably with *E. histolytica* of Schaudinn. The description of the amœbæ is very detailed and precise, and apparently agrees minutely with the characters, such as the form, appearance, and position of the nucleus, advanced by Schaudinn to separate the pathogenic *E. histolytica* from the harmless *E. coli*. The absence of any reference by such careful observers to the formation of cysts, which is easily observed in *E. coli*, must be regarded as confirmative evidence of the presence of the other species. If this opinion with regard to the identity of the forms proves to be correct, the specific name given by Councilman and Lafleur will have to be used in preference to the later form given by Schaudinn and the species will be known as *E. dysenteriæ* (Councilman and Lafleur 1891). Although illustrated by very inadequate figures, the pathological lesions caused by this species are described by these authors with great fulness and care, and anticipate very largely the work of Jürgens, to which Schaudinn accords such well-merited praise.

The following forms included under the generic name *Amœba* are classified thus rather tentatively, as our knowledge of the life history at least is too limited to allow of greater precision. Probably some at least are related to the species just described if not identical with them.

Amœba Miurai Ijima 1898.—Normally isolated individuals (Fig. 5166), adhering in conglomerate-like clusters only when dead or dying. Living specimens, spherical or ellipsoidal, having at one pole a small rounded protuberance or villous knob, which is closely set with fine pseudopodia. Diameter 0.015–0.038 mm. Villous knob papilliform or hemispherical, 0.01 mm. in diameter at base, but capable of entire retraction at times, or the fine pseudopodia may be entirely withdrawn. Nucleus round, oval, or reniform, 0.008–0.015 mm. in diameter, two or three being found in the single cell as often as one. Ectoplasm visible only in villous knob; endoplasm finely granular with one to several conspicuous non-contractile vacuoles and minute oil-like corpuscles.

This form was found by Miura and described by Ijima. It occurred in the serous fluid accumulation of peritoneal and pleural cavities in a female, twenty-six years old, who died from peritonitis and pleuritis endotheliomatosa. The amœbæ were absent at first from the fæces, but made their appearance two days before the patient's death, concomitantly with hemorrhage in the intestine. Living and dead individuals were found together in the freshest serous fluid under rigid precautions against injurious influences, and this is regarded by Ijima as evidence of the abnormal occurrence of the parasite. It has not been reported since then, and is explained by some authors on the basis that the supposed amœbæ were only "exudate cells." Lühe states that this is unquestionably the case.

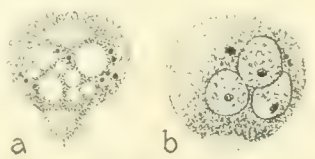


FIG. 5166. *Amœba Miurai*. *a*, Living; *b*, from specimen preserved in acetic acid. 500. (After Ijima.)

A considerable number of so-called amœbæ have been reported from various organs in man, and usually pathogenic characteristics have been attributed to them. They are known mostly from single records of their occurrence, and often lack both name and recognizable description. It has been suggested that they are commensals, and of secondary importance. It is equally probable that some at least are occasional or accidental parasites, and devoid of general importance in human pathology. Owing to the general uniformity of structure in this group all but the most careful descriptions are worthless for future study and comparison with other species. A few of the best accounts of these uncertain forms are noted here for reference.

Amœba Kartulisi Doflein 1901.—Diameter 0.03–0.038

[illegible] without distinct ectosarc and endosarc. Plasma coarsely granular, with very small [illegible] nucleolus demonstrable only by special [illegible]. Movement more rapid than in [illegible]. Encysted forms occur; a few pseudopodia may develop during encystment. Reproduction not observed.

This species was found by Kruaths in Alexandria, where it occurred in an Arabian, in a tumor the size of [illegible] in the thick pus and on [illegible] the amœbæ occurred together with numerous bacteria. They had been feeding on blood and pus corpuscles. Although apparently distinct from *Entamœba coli*, Doflein inclines to regard their connection as not impossible, and views as even more probable this interpretation of the amœbæ from an abscess in the oral cavity reported by Flexner. These were described as larger than leucocytes, with granular vacuolated plasma and a nucleus demonstrable only with some uncertainty. Although in both these cases the presence [illegible] in the host had not been shown by any antecedent dysentery or fæcal examination, it has already been stated that this species may be present in the normal intestine, and its occurrence outside the canal in abscesses is abundantly demonstrated by other cases. It is less probable this form may have been *Entamœba histolytica*, though the description is not distinctive, as the absence of lesions in the canal can hardly be explained if the pathogenic species was present.

[illegible] *tenuis* Badz 1883.—Diameter 0.022–0.05 mm. Plasma coarsely granular, containing one or several nuclei, excretory products, and erythrocytes. Movement slow, by formation of short pseudopodia. Encysted forms possibly occur.

Originally found in numbers in the bloody urine and vaginal mucus of a Japanese female, twenty-three years old, who shortly before her demise from tuberculosis manifested hæmaturia with strong cystic tenesmus. (*Cf.* Vol. I., p. 233, HANDBOOK.) Similar cases have been reported by many authors. In Jürgens' case chronic cystitis was associated with small mucous cyst filled with amœbæ; these were also present in the entire vagina. The descriptions are scanty and do not render a differentiation between these forms and *Entamœba coli* and *E. histolytica*, either structurally or clinically easy at present. Pathogenic characteristics are certainly not distinctly shown, and in so far this case belongs more probably to *E. coli* if to either. Better knowledge of the species and more careful examination of the reports of previous observers may make it possible to refer some such cases to a definite species; but many will always remain uncertain.

Amœba buccalis Sternberg 1862; *Amœba dentalis* Grassi 1879; *Amœba gingivalis* Grassi 1849.—All these species were discovered in tartar scraped from the surface of human teeth. They have not been reported a second time, and Celli and Fiocca state specifically that they have failed to find amœboid organisms in the oral cavity. Grassi himself suggested the possibility of confusion with salivary corpuscles.

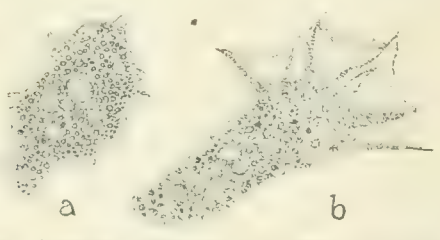


FIG. 5166. *Leydenia gemmipara*: *a*, at rest; *b*, in movement. Magnified. (From Doflein after Schaudinn.)

Amœba pulmonalis Artault 1898.—In an examination of the contents of a large pulmonary cavity a small number of amœbæ were found among the leucocytes, which were distinguishable by firm contour, much finer and more uniform granulation, and a distinct nucleus or vacuole. In appearance like the epithelial cells found in sputum they manifested changes in form and position through the slow formation of pseudopodia. They were also more highly refractive, and resisted methylene blue or fuchsin longer than leucocytes, but when preserved they stained readily and were indistinguishable from the latter. Despite the conjectures of the discoverer their real nature remains entirely unknown.

Leydenia gemmipara Schaudinn 1896.—Irregularly spherical or polygonal in form when resting (Fig. 5167, *a*), surface with prominent verrucosities. Ectosarc and endosarc not distinctly limited, but pseudopodia more hyaline than the opaque body with numerous highly refractive yellowish granules. Diameter of body, 0.003–0.036 mm. Nucleus single, spherical, distinct in life, and in the preserved specimen regularly one-fifth the diameter of the body; movement very slow, produced by formation of a broad, hyaline lamella at the anterior margin; streams of granular endosarc extend to the margin of this lamella (Fig. 5167, *b*), and may even project beyond it as pointed pseudopodia. The endoplasm contains granules, crystalline bodies, interpreted as excretory, and numerous vacuoles which increase in size toward the centre. A pulsating vacuole is present and contracts at intervals of about fifteen minutes.

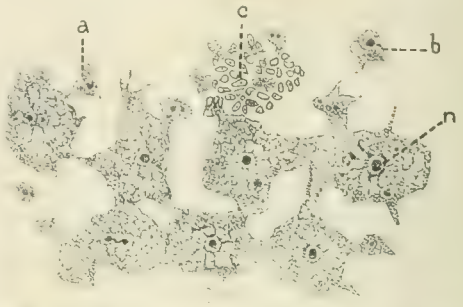


FIG. 5167. *Leydenia gemmipara*. *a*, *b*, *c*, Young individuals formed by gemmation. *n*, nucleus. Magnified. (From Doflein after Schaudinn.)

Two or more individuals frequently unite without fusion of the nuclei, and plasmodia are formed by the union of many single individuals. Both division and gemmation occur. In the former the size of the resulting amœbæ may be very different, but is always proportional to the size of the nuclei (5:1). The nucleus divides directly, and the bud which originates as a protuberance from the surface of the amœba gradually works free and becomes an independent individual, which may at once undergo multiple division, giving rise to a mass of small spore-like forms (Fig. 5168).

Many years ago Lieberkühn observed in ascites fluid associated with malignant tumors peculiar cells; and similar structures were seen later by others. In 1896 Leyden and Schaudinn, on the basis of an exact investigation of these bodies in a particular case, determined them as a new parasitic rhizopod. Leyden had found them in the ascitic fluid of two patients in whom positive evidence of gastric carcinoma and of tumors in the peritoneal cavity was furnished. The amœbæ appeared in numbers in fluid drawn off from the cavity, and could be kept alive in fluid preserved several days under aseptic conditions. Schaudinn studied the amœbæ carefully and pronounced them to be unmistakably parasitic forms. Some later critics have inclined to reject this view, and regard them as descendants of the human tissue cells or pathologic neoplasms. L. Pfeiffer especially has maintained that similar large amœboid cells ("exudate cells") occur in variola, vaccinia, varicella, herpes zoster, etc., and yet the contractile vacuole, peculiar nuclear structure, and reproductive processes of *Leydenia* indicate unmistakably an independent organism, as well as many other features in which it resembles various related free-living forms.

Originally Leyden and Schaudinn were inclined to connect this form with carcinoma but expressed no positive opinion on this point. Unfortunately it has not been studied by subsequent investigators, and in fact has been found but twice since then, although often sought for under similar circumstances. Recently Schaudinn has advanced the view that this form is probably an accidental commensal.

The class of the Mastigophora includes a great variety of organisms, having in common hardly more than the possession of vibratile organs of locomotion known as flagella, which by greater length, lesser number, and type of movement are easily distinguishable from cilia. The group shows relationships in many directions and affords an almost unbroken line of transition to forms which are typically plant organisms. Here, again, as in the last class (Sarcodina) the uniformity of structure, coupled with an even smaller average size and very insufficient acquaintance with the life history, render it difficult to speak positively regarding many of the organisms. Of the sub-classes, which are founded upon the number and arrangement of the flagella, the character of the cell body and general habits of life, only one, Flagellata, is of importance here, as the others contain no parasitic forms.

The general form of the body, the number and position of flagella, and the precise method of reproduction serve to distinguish in the sub-class Flagellata five orders. Only two of these embrace human parasites and demand consideration here, namely: Protomonadina and Polymastigina.

The Protomonadina are small forms, often tending to form colonies. They have at the anterior end one flagellum, two similar flagella, or two or three dissimilar flagella. In many parasitic species an undulating membrane accompanies a single flagellum. Doflein gives the following key for the determination of those families which include parasitic species:

1. A single flagellum on anterior end 2
   Two flagella on anterior end ..... Bodonidæ
2. An undulating membrane along the side of the body ..... Trypanosomidæ
   No undulating membrane present .. Cercomonadidæ

Cercomonas.—The species in this genus are rather uncertain. Many forms have been assigned to it which later studies have shown to belong to other genera. Confusion is possible both with plant organisms and with mere developmental stages of other groups. The species are small and colorless; in form round or oval, with a very large flagellum, which is projected ahead in locomotion. Many of the forms reported from the human body and assigned to this group are imperfectly known, often found but a single time, and in many cases probably pseudoparasites of various degrees. One or two of the more distinct forms need brief mention here.

Cercomonas hominis Davaine 1854.—Body pyriform, pointed posteriorly, with single flagellum at anterior end. Length 0.01–0.012 mm. Movement rapid, capable of attaching themselves by posterior tip. Smaller variety 0.008 mm. long.

Found in the dejecta of a cholera patient, the smaller variety in typhoid dejecta. Various later reports may be assigned to this species, including that of Lambl in 1875, which has often been erroneously identified as the same as the species described under the same name by this author in 1859. The latter will be discussed under its present name of *Lamblia duodenalis*. Some authors have assigned the former species to *Trichomonas*, forgetful of the fact that it possesses but a single flagellum.

It would be hazardous to assert that all typical cercomonads thus far described from the human host fall unquestionably into the limits of a single species; yet in the absence of contradictory evidence they may for practical purposes be considered as such. These forms have been found in the alimentary canal, the bronchial system, in pleural exudate, and in an *Echinococcus* cyst. Encysted forms have also been described. All investigators have not been equally careful to demonstrate the intestinal origin of such forms as were found in fæces, and which may have been due to secondary contamination of the fæcal material. Among numerous records only those of Councilman and Lafleur and of Dock concerning the occurrence of such forms in this country need be mentioned.

Monas pyophila R. Blanchard 1895. (Syn.: *M. pyophyla* Neveu-Lemaire 1902.) Form similar to large spermatozoa, 0.03–0.06 mm. in diameter of body, with long filament from rounded pole, resembling a flagellum, yet capable of retraction when the form becomes nearly spherical. Outside a cuticular (?) layer, which extends through the body in partitions, dividing it into three regions. Movement rapid, accompanied by change of form.

Found by Grimm in sputum and pus of abscesses in lung and liver of patient in Japan.

The Trypanosomidæ are parasitic forms with a chief flagellum directed anteriad, usually two-edged, with more or less of a spiral twist in the body, and with one edge of the body provided with an undulating membrane. The numerous species are hæmatozoa in vertebrates, though some live in the body cavity and alimentary canal of both vertebrates and invertebrates. Those forms of importance here all fall in the genus *Trypanosoma* s. str. Much difference of opinion prevails as to the number of species and their limits. Most of them are very poorly known, although several so-called species were discovered as much as sixty years ago; indeed of no form is even an approximately complete account of the life history at hand. Various species are recognized in various parts of the world as the cause of specific diseases among domesticated animals, which have assumed economic importance of the first rank. The most prominent of these are the following, together with the range and host of each species listed.

Trypanosoma Lewisi, in rats and (?) the hamster, reported from Europe, Asia, Africa, and North America, and causing at times fatal epidemics.

Trypanosoma Brucei, in cattle, horses, mules, and wild animals, gives rise to the *nagana* or Tsetse-fly disease in Africa south of the Sahara.

Trypanosoma equiperdum, in horse, ass, and other domesticated species by inoculation, causes *dourine* in the circum-Mediterranean region.

Trypanosoma Evansi, in mammals, especially domestic, where it causes the *surra* in India, China, Burmah, and the Philippines.

Trypanosoma equinum, in horses, causing *mal de caderas* in South America.

Trypanosoma Theileri, in cattle, producing the *galziektè* in South Africa.

Although but little evidence is at hand, the weight of opinion is against any possibility of the transmission of these species to man.

Some structural features of the genus *Trypanosoma* s. str. need brief mention. The lancet-shaped body (Fig. 5169, *a*) shows a finely granular endoplasm and a distinct

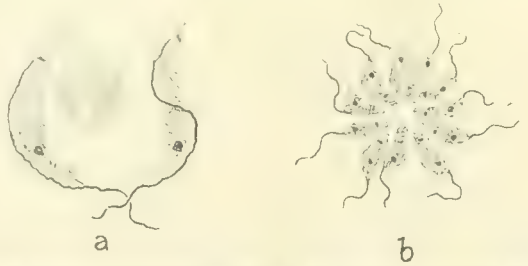


Fig. 5169. *Trypanosoma Lewisi*. *a*, Adults with erythrocyte, from stained preparation. 1,000. *b*, Multiplication rosette, less highly magnified. (After Francis.)

though very delicate hyaline ectoplasmic layer. The single flagellum arises near the posterior end in connection with the highly refractile granule variously denom-

inated centrosome, micronucleus, and nucleolus. The flagellum continues along the body as the thickened outer margin of the undulating membrane, and projects free from the anterior end of the animal. The prominent

Fig. 5170.—*Trypanosoma Lewisi*. Auto-agglutination. Highly magnified. (After Francis.)

nucleus occupies a slightly different position in different species; it is rich in chromatin and stains deeply in prepared specimens.

Three types of reproduction are imperfectly known: a typical longitudinal division, a budding said by Senn to be more common, and a segmentation or multiple division into numerous spores (?) arranged in rosettes (Fig. 5169, *b*). The rosette formation is regarded by some authors as the result merely of the successive division of an ordinary individual of the species. These rosettes of enormous size, embracing several thousands of individuals, occur characteristically in cultures of *Trypanosoma Lewisi* (Fig. 5170). Such cultures have been recently successfully obtained by McNeal and Novy in a strictly pure form, and have been maintained for somewhat over a year. The great importance of this step for the study of the pathogenic activity of the organism and of the possible protective measures in combating the disease is evident at once. The species found in man is

Trypanosoma gambiense Dutton, 1902. (Syn.: *T. hominis* 1902, ? *Nepveu* Sambon 1903.) Length in stained preparation (Fig. 5171), including flagellum 0.018–0.025 mm., width 0.002–0.0028 mm. Free part of flagellum about one-third of total length. Anterior end attenuated along flagellum, posterior end roughly conical, very blunt. Oval macronculeus just anterior to centre of body, occupying entire width of animal. Near posterior end dark spot, the micronucleus (the centrosome of Laveran and Mesnil), and just anterior to it a large vacuole well marked. The flagellum ends at the upper edge of this vacuole. The first record of the occurrence of a trypanosome in man is said to have been published by Nepveu in 1891, and again in 1898. The description given, however, is too scanty to admit of any opinion regarding its general character, though many are inclined to interpret it as a member of the genus *Trypanosoma*. This species was discovered in 1901 by Dutton in the

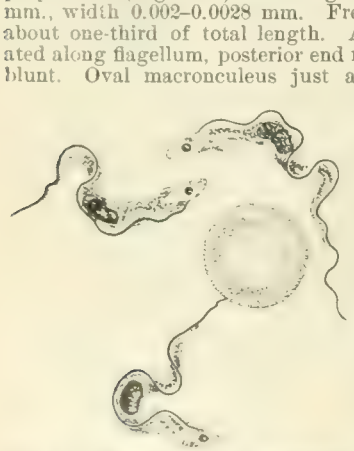


Fig. 5171.—*Trypanosoma gambiense*, with central cyst, drawn from stained preparation. (About 1000. After Dutton.)

blood of an Englishman in government employ on the Gambia River. The case was under observation some time, namely, until the patient died in January, 1903, and manifested the following clinical features: general weakness, irregular lapsing fever lasting one to four days with apyrexial periods of two to five days, some œdema, injection of the skin, enlargement of the spleen, constant frequent pulse, and hurried breathing. These symptoms were associated with no definite organic lesions.

In many prepared slides and fresh blood mounts there were found no malarial organisms. The number of trypanosomes present varied from one to fifteen, but in apyrexial periods none were detected in the blood. The parasite usually progressed with the flagellum in front, but occasionally reversed direction for a short distance. In slow progression wave-like motions start in the flagellum and are communicated to the undulating membrane; in rapid motion the body rotates on its longitudinal axis so that the undulating membrane appears as if spirally arranged. In one instance a mononuclear leucocyte was observed which had partially engulfed a trypanosome, only the flagellum and a small part of the anterior end of the body remaining free.

In films of blood taken from a child three years old the parasite was discovered again and associated with it malarial organisms. Annett points out that the chronic character of the disease, the rarity of the parasites, their apparent absence at long periods from the peripheral circulation, and the occasional rise in temperature favor confusion with malaria in diagnosis.

Later further cases of the malady have been identified by Dutton, Manson, and others, making in all six cases on the Congo River and seven on the Gambia, which are nearly equally divided between natives and Europeans. It is thus evidently not rare in tropical Africa, as Dutton found his seven cases in somewhat more than one thousand examinations in Senegambia. Two investigators seem to have identified it in India also, and it may be expected to occur in other countries as well, as do the corresponding affections of domestic animals.

A final most recent contribution of great importance to this subject has been made by Castellani, who found *Trypanosoma* in the cerebro-spinal fluid of natives afflicted with the so-called "sleeping sickness." This hitherto entirely unexplained disease, epidemic in certain regions of Africa, attacks only natives, and is characterized by a drowsy condition culminating in deep coma, with an all but universally lethal outcome in from three to twelve months. Hyperæmia of the arachnoid vessels is the only known pathological feature. Bacteriological investigations have remained without result, and the theory of Manson that the cause of the malady lay in the presence of *Filaria perstans* has already been referred to in another article (*Nematoda*). Castellani's hypothesis has been greatly strengthened by the communication of Bruce to the Royal Society that *Trypanosoma* was present in the cerebro-spinal fluid in every one of thirty-eight cases of sleeping sickness investigated in Ugunda, and occurred also in the blood in twelve out of thirteen cases tested on this point.

This species, which has been named *Trypanosoma Castellanii* (see Sambon in *Journal of Tropical Medicine*, July 1st, 1903), closely resembles *Trypanosoma Brucei*, but is said to differ in the following morphological peculiarities: a more or less rounded anterior extremity (posterior extremity of most authors, but this species moves with the more rounded extremity foremost), the centrosome outside the vacuole and much closer to the extremity, the larger vacuole placed before (?) the centrosome, the longer free portion of the flagellum and fewer granules at the posterior extremity.

The transference of the parasite is probably due to some blood-sucking insect, as has been demonstrated for other species of *Trypanosoma;* and in the case of the sleeping sickness, *Glossina morsitans*, the Tsetse fly has been declared responsible by Brumpt. In an illuminating discussion of the subject he shows that the disease is ex-

traordinarily widespread among fishermen on the Congo, and almost unknown among people in the vicinity, who yet do not visit the stream. This accords with the habits of the Tsetse fly, which occurs on the river in immense swarms and is not found a short distance away from it. The freedom from this disease enjoyed by the whites can only be explained on the basis of present knowledge as a type of racial immunity. Recent observations, however, serve to arouse suspicion as to the correctness of the assumption itself.

Although the morphological differentiation of the various species of *Trypanosoma* is difficult, not to say impossible at present, there are sufficient grounds in the clinical features of the diseases caused by them, and in other physiological data, such as the immunity of various host species to certain forms, to justify the acceptance of their specific distinctness. One may well recall the earlier view, that only one form of malarial organism existed, and may find in the transport by *Anopheles* of different species of *Plasmodium* a case parallel to that of the Tsetse fly. Whether the latter host affords the opportunity for the development of a special phase in the life cycle of the trypanosome is as yet purely a matter of conjecture.

The family of the Bodonidæ would not call for any discussion here were it not for the frequence with which certain species have been assigned a rôle as parasites of man. The form which has most frequently been mentioned in this connection is

Cystomonas urinaria (Künstler 1883).—(Syn.: *Bodo urinarius* Künstler 1883; *Cystomonas urinaria* Blanchard 1886; *Plagiomonas urinaria* Künstler of Braun 1895.) Shaped like a beet root (Fig. 5172), 0.01 mm. long, 0.004–0.005 mm. broad, the broad anterior end notched, the posterior end in the form of a long slender filament. Nucleus anterior; two similar flagella originate from anterior notch.

In 1856 Hassall described an infusorian which he had observed in alkaline urine that had stood some time open to the air. It was subsequently found in fifty samples of urine from various sources left open similarly, sufficient proof of the contamination. In 1883, however, Künstler reported a form under the same name from fresh urine, which was accordingly attributed to the urinary passages. Blanchard held this to be in reality a new species and renamed it, bringing it in connection with a form described by Salisbury as *Trichomonas irregularis*. Braun regards the latter as rather *Tr. vaginalis*, and distinct from the former, for which he inclines to the view that it was actually a contamination. This is the more probable, as Th. Barrois found many flagellates in "freshly voided" urine in Lille, when subsequent examination yielded no trace of these parasites in urine of the same patients. Evidently the presence of such forms in human urine is beyond question, but their origin from the human urinary passages is yet to be demonstrated. That all such cases require the most searching examination is evinced by a recent experience of my own, in finding objects which were probably much contracted rotifers in preparations made from "absolutely fresh" urine.

FIG. 5172.—*Cystomonas urinaria*. Magnified. (From Braun, after Künstler.)

The order Polymastigina includes small forms, always non-colonial, with three similar flagella, or with four to eight flagella dissimilar in size and differently located. Two families contain parasitic forms and are distinguished as follows:

Body with three or four flagella, all at anterior end ..... Tetramitidæ

Body with four to six flagella on anterior end; posterior end either with two flagella, or prolonged into one to three lobes ..... Polymastigidæ

In the Tetramitidæ are included species of elongated form with usually pointed posterior end. They have no cuticula, or pellicle, hence may also manifest amœboid movements. One of the flagella may be represented by an undulating membrane. Only one of the genera, *Trichomonas*, embraces human parasites. The diagnosis of the genus may be given briefly as follows:

Trichomonas Donné.—Generally pyriform, with anterior end rounded or almost pointed. Posterior end moderately pointed. Nucleus near anterior end, vacuoles near posterior, no contractile vacuole. Either three equal flagella from anterior tip, and also an undulating membrane (*Trichomonas* s. str.), or with three equal flagella directed anteriad, and one much longer extending posteriad from the same point of insertion (sub-genus *Trichomastix*).

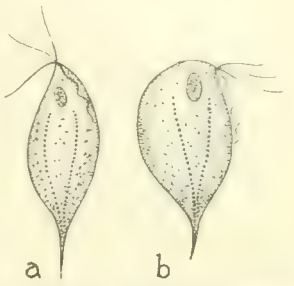


FIG. 5173. *Trichomonas vaginalis*. *a*, From osmic-acid preparation; *b*, living. Magnified. (After Blochmann.)

Trichomonas vaginalis Donné 1837.—Body very mobile, usually pyriform or spindle-shaped (Fig. 5173), with posterior end sharply pointed and anterior end more or less rounded. The posterior tip is half as long as the rest of the body. Total length 0.015–0.025 mm. At anterior pole originate three flagella (four according to other investigators) of equal length, and an undulating membrane which winds spirally about the body to the base of the posterior tip. Plasma finely granular, nucleus near anterior end; posterior to it according to Blochman two longitudinal rows of prominent granules. Division has been reported; encystment is as yet unobserved.

This species is present in females where vaginal catarrh is associated with an acid reaction of the secretion. It has been found in girls of six or seven years and in aged women; and other conditions affect its presence as little as age save that menstruation, alkaline injections, or other conditions which alter the reaction of mucus result in its disappearance temporarily at least. A low temperature (15° C. or less) is also fatal to its existence. Dock and others have demonstrated the presence of this species in the urine of males; the infection doubtless resulted from intercourse and was made possible by an already abnormal condition of the male urethra, as was shown in the cases under discussion. Dock was unsuccessful in infecting guinea-pigs and dogs, and the means of transference from one female to another is unknown. According to Hausmann thirty to forty per cent. of females are infected. The parasites are easily demonstrated in the vaginal mucus, where they move slowly about among epithelial fragments and mucous corpuscles; but for successful demonstration the urine must be examined as soon as passed. Whether their relation to the vaginal catarrh is primary or secondary remains entirely undecided.

*Trichomonas intestinalis** (R. Leuckart 1879).—(Syn.: *Protoryxomyces coprinarius* Cunningham 1881; *Monocercomonas hominis* Grassi 1882; *Cimænomonas hominis* Grassi 1882; *Trichomonas hominis* Grassi 1888; *Cercomonas coli hominis* May 1891; *Monocercomonas hominis* Epstein 1893.)

Very similar to *Tr. vaginalis* but smaller, measuring 0.004–0.015 mm. in length and 0.003–0.004 mm. in breadth, without rows of granules; posterior end more sharply set off and measuring only one-third the length of the body. Three flagella, the free edge of the undulating membrane has sometimes been interpreted as a fourth. Otherwise as in *Tr. vaginalis*, although the species has not been carefully investigated. Kruse and Pas

* This form of the name is probably incorrect, but as the synonymy is badly confused I have retained it pending revision by some specialist.

quale observed groups of individuals which may have arisen by division. Before copulation this species loses its flagella and creeps about with bluntly lobose pseudopodia. This species is ordinarily identified as the *Cercomonas hominis* of Davaine (1854) and the *C. intestinalis* of Lambl (1875), but recent studies have demonstrated the individuality of this from the two cited. There also is a tendency at present to reduce this form to *Tr. vaginalis*, with which it agrees closely, and only an exact study can decide the question. In the uncertainty I regard it as more practical to retain both species, though they are at least closely related.

Tr. intestinalis parasitizes in the anterior and middle regions of the human alimentary canal, and has been repeatedly found in various parts of the world. It occurs also in the oral cavity in decaying teeth, where it nourishes itself on micrococci. It has been reported also frequently from diseased conditions associated with diarrhœa, such as typhoid, cholera, intestinal catarrh, gastric carcinoma, and once in pulmonary gangrene. The species lives only in fluids of an alkaline reaction. Its occurrence in the dejecta of healthy adults has been taken to indicate a commensal rather than a parasitic habit; but it at least multiplies rapidly in connection with morbid processes, and this may exercise an important influence on the progress of the disease. An etiological significance cannot, in the present state of knowledge, be attributed to this species; yet the experiments of Epstein showed that an infection is apparently produced by drinking-water and followed by diarrhœa in children. Experimental infection of animals has not yet succeeded, and the presence of this species in the oral cavity, both in health and in disease, points to possible transport of unknown encysted forms by the air.

Some accounts referred to supposable new species more probably concern this. Such are the forms described by Steinberg from the oral cavity as *Tr. elongata*, *Tr. caudata*, *Tr. flagellata*, as well as perhaps also *Cercomonas biflagellata*, together with the *Tr. pulmonalis* of Schmidt and Artault from sputa or contents of a pulmonary cyst.

The family Polymastigidæ contains small biaxial or bilateral forms with two or three flagella on either side or near the anterior end, while the posterior end is lobed or provided with two further flagella. Only one genus contains human parasites.

Fig. 5174. *Lamblia duodenalis*, Living, from Rabbit Intestine. Magnified. Combined sketch. After Metzner.)

Lamblia Blanchard.—At anterior tip one flagellum on each side, and near the centre two on either side; posterior end with two additional flagella. A concave sucking disc (?) on ventral surface near anterior end. Nucleus dumbbell shaped.

Lamblia duodenalis (Davaine 1875).—(Syn.: *Cercomonas intestinalis* Lambl 1859, nec 1875 nec Perty 1852; *Hexamitus duodenalis* Davaine 1875; *Dimorphus muris* Grassi 1879; *Megastoma entericum* Grassi 1881; *M. intestinale* R. Blanchard 1886; *Lamblia intestinalis* R. Bl. 1888; *L. duodenalis* Stiles 1902.)

Length 0.01–0.016 or 0.021 mm.; maximum breadth 0.005–0.007 or even 0.012 mm., with eight flagella nearly equal in length (0.009–0.014 mm.). In form bilaterally symmetrical (Fig. 5174). In ventral aspect it is rounded anteriorly and prolonged posteriorly into a very mobile steering tail flattened in the frontal plane. A shallow cordiform excavation of the ventral surface near the anterior end corresponds to the peristome and serves as an organ of attachment; its margin is raised and contractile, but is interrupted posteriorly; all flagella point posteriad; the anterior pair follow the margin half-way around before leaving the body; the lateral pair originate near the anterior margin in the peristome, but are bound to the body until they come to project beyond the contour of the animal; the median pair originate in the notch of the peristome margin and are vibratile through their entire length, being the chief organs of locomotion; the caudal pair are inserted at the tip of the body. The dumbbell-shaped nucleus lies dorsal to the peristome. Contractile vacuole and cytostome are wanting. Division has not been observed; the encysted form is oval, with heavy transparent wall, and measures 0.01 mm. in length by 0.007 mm. in breadth. Schaudinn reports that copulation has been observed and is followed by encystment.

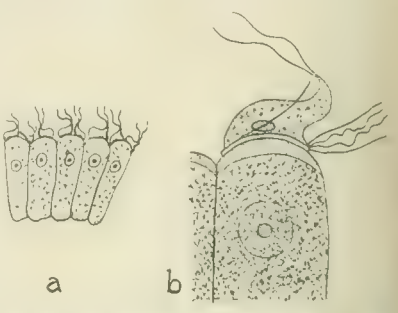


Fig. 5175. *Lamblia duodenalis*. *a*, On epithelial cells of intestinal villus. × 350. *b*, single cell and parasite. × 1,070. (After Grassi and Schewiakoff.)

This species was first reported by Lambl from the dejecta of children in Prague. It has been reported from Germany, Italy, Russia, Sweden, Egypt, and the United States from the human host in which it seems to be a frequent parasite. It also occurs in rat, mouse, dog, cat, rabbit, sheep, and certain wild species, and is undoubtedly a common and widely distributed parasite.

Its normal seat is the duodenum or jejunum, rarely other parts of the canal, where it sits with the peristome applied to the curved outer face of an epithelial cell (Fig. 5175) on the villi. Although often in such numbers that apparently every cell is occupied, yet no pathological effect has been demonstrated to be exercised by these parasites. Normally only cysts occur in the colon and fæces, but in diarrhœic conditions the free living forms are torn loose and reach the exterior.

Grassi determined by experimental auto-infection that the cysts are the means of infection, and was unable to detect in himself any symptoms incident to the parasitism of the species. It is probable that cereals, or prepared food which becomes contaminated by rats or mice, constitute the ordinary avenue by which the infection of man is brought about.

The class Sporozoa embraces a series of groups of Protozoa of a consistent parasitic habit, which have in common the production at some point in their life cycle of numerous descendants, which are usually covered by a firm shell and accordingly denominated "spores." The enclosed young forms may be single or manifold, and in special cases the cyst wall may be lacking. These young forms always start the life cycle as cell parasites, and in all but rare cases alternation of generations appears in the course of the life history. All forms are true parasites, and all subsist only on fluid nourishment obtained by osmosis.

The class was made by Leuckart in 1879, when he brought together under the heading Sporozoa the imperfectly known and somewhat isolated groups of gregarines (Gregarinida), the psorosperm sacs of Müller (Myxosporidia), the oval or spherical psorosperms of Eimer (coccidia), and Rainey's or Miescher's corpuscles (Sarcosporidia). Later investigators have added the Microsporidia, Amœbosporidia, and Hæmosporidia, and have been able to fill up the gaps in the knowledge of the older groups, so that the association of these forms stands on a much clearer and firmer basis. This is especially true by virtue of the recent discoveries concerning the life cycles of va-

rious forms which have revealed an entirely unsuspected complexity and interrelation of the development with the parasitic habit.

In the majority of cases two types of reproduction alternate in the life history of the organism, and this alternation is associated with different factors in the biology of the parasite. The first type subserves the rapid multiplication of the parasite within the host, and is appropriately designated by Doflein multiplicative reproduction; when highly developed it will evidently transform an organism harmless because insignificant into an abundant destroyer of tissue and the exciter of disease. This may be observed again and again in the account of this group. The other type of reproduction is connected with the spread of the species, the infection of new hosts, and may be denoted after Doflein the propagative reproduction. Spore formation is here associated with all sorts of secondary or collateral structures which assist in the transport of the spores, their protection during this period, and their attainment of the new host. The morphology of the propagative reproduction constitutes the means of characterizing the major subdivisions of the Sporozoa; the multiplicative reproduction varies often widely among closely related forms.

The two sub-classes, Telosporidia and Neosporidia, are distinguished by the fact that the former produces spores only at the close of the vegetative period, while the latter do so during the entire period. For the identification of a sporozoon a vegetative stage is rarely sufficient; the form and number of the spores produced during the propagative period of reproduction are characteristic.

In the sub-class Telosporidia one may distinguish two orders on the basis of the habit of the parasites and the mode of fertilization which prevails. Thus in the Coccidiomorpha the vegetative stage is permanently intracellular, while the sexual generation may be so only transiently. The fertilization is anisogamous, *i.e.*, the fusion of differently formed gametes. In the Gregarinida on the other hand, the vegetative stage is intracellular only at the start, as the adult organism is extracellular and the sexual generation also. The fertilization is isogamous, *i.e.*, the fusion of equal and similar gametes. Under the order of the Coccidiomorpha are included forms which until recently have been treated as much more distinct. But more careful study, particularly of the life history, has shown an increasing degree of likeness until they are now included in the same order, and mutally opposed to the Gregarinida in the specific cell parasitism, and in a similar alternation of generations and of hosts in addition to the features pointed out in the outline of the system given above. The features which serve to distinguish the two sub-orders of the Coccidiomorpha are these: The Coccidia produce sporozoites encased in sporocysts, with the exception of *Legerella*, the copula is non-motile and remains in the cell. In the Hæmosporidia the sporozoites are always free, the copula is an active ookinet, and migrates to a new location before undergoing further development.

The adult Coccidia occur as parasites in epithelial cells, particularly of the alimentary canal and its adnexa, though the excretory organs, the male sexual organs, and most recently the spleen are also reported as affected. While the protoplasm of the host cell is ordinarily the seat of the parasite, there are not wanting such as occur in the nucleus itself. Only rarely is more than a single parasite found in an epithelial cell.

In form the Coccidia are uniform and constant, being spherical, oval, or elliptical, and without organs of locomotion of any sort or organs of attachment. Their size is regularly insignificant. A noteworthy characteristic is the absence of differentiation into ectoplasm and endoplasm. The plasma of the cell is finely granular, alveolar, and without reserve bodies or food vacuoles. The nucleus is large, vesicular, and characterized by a single prominent central nucleolus. No contractile vacuole is present, and no further structural differentiations can be noted. The cell and nucleus increase gradually in size at the expense of the host cell, which ultimately in most cases degenerates to a mere empty membrane encircling the coccidium.

The nucleus of the now full-grown parasite undergoes multiple division, the protoplasm arranges itself in individual masses about the many daughter nuclei, and there results a stage in which a rosette of young forms (Fig. 5176) encircles a central portion of protoplasm, known as the reliquary body or residual mass. This is without nuclear matter and destined to play no further part. It is left behind, and perishes when the young forms wander out to infect new epithelial cells of the same host, and repeat the process just sketched. This is evidently the multiplicative reproduction already referred to. It serves to effect the auto-infection of the host, and is generally known as the period of asexual reproduction or schizogony. The cell parasites which undergo these changes are schizonts, while the young forms are denominated merozoites. The merozoites are capable of active movements by contraction and twistings, or with a gliding movement, in which a trail of mucus is left behind. The growth of merozoites to schizonts in the epithelial cells, the production of new merozoites, and the infection of new cells proceed often with considerable rapidity, but only within certain limits, for a new type of reproduction intervenes.

In this which regularly begins under the pressure of excessive infection of the host, the merozoites develop not to schizonts, but to forms of two sorts, which at first sight are very similar to schizonts, and but little different from each other. The one form is opaque with a richly granular plasma; the other has a clear but dense plasma. The opaque form is the female gamete, or macrogamete, and attains maturity by the rejection of a portion of its nuclear substance. The clear cell, known as a microgametocyte, undergoes multiple nuclear division. The many nuclei produced then migrate to the surface, each collects a small part of the plasma about itself, and projects as an elongated spindle-shaped structure, the microgamete or male cell, which becomes free, forms two flagella, and enters upon active locomotion. The major portion of the microgametocyte is abandoned, and subserves no further function.

FIG. 5176. *Eimeria Stiedæ*. Adult Schizont Completely Divided into Merozoites. Cyst formed of degenerated host cell is not represented. Magnified. (After Simond.)

The microgametes swarm about the macrogametes, and as soon as one has succeeded in entering, the macrogamete forms at once a firm membrane, which forbids entrance to other microgametes. The two nuclei unite and the act of fertilization is completed. The product is known as an oocyst, copula, or sporont, and forms the starting-point of a new period in the life cycle, which is that previously designated as the propagative reproduction. It is also known as the sexual spore-forming period, or sporogony, and in most coccidia takes place

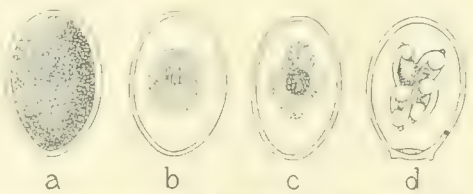


FIG. 5177. *Eimeria bovinus*. Spore-story. *a*, *b*, Oocyst; *c* sporoblasts with residual mass; *d*, sporocysts with contained sporozoites. Magnified. (From Braun after Riek.)

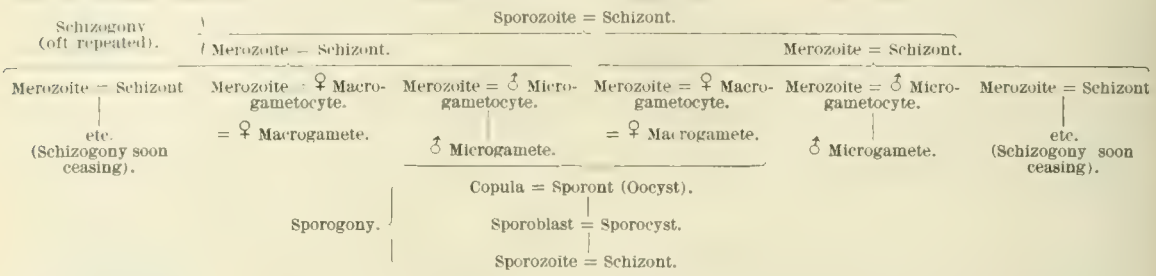
outside of the host, after the oocyst has been evacuated in fæces or urine. The steps in the process of sporogony may be outlined next in general terms (Fig. 5177).

The nucleus of the oocyst (*a*) divides twice, and about the four daughter nuclei the protoplasm separates into four parts known as sporoblasts (*b*), and sometimes also

a residual mass of protoplasm (*c*). Each of these sporoblasts surrounds itself with a firm membrane and becomes a sporocyst (*d*), while later within each sporocyst after nuclear division two sporozoites are formed and a residual mass of protoplasm is left unused. The sporozoites are characteristically sickle-shaped or crescentic, and abandon the sporocyst when this reaches the alimentary canal of the new host, and is opened by the action of the alimentary secretions. The entrance of the sporozoites into the epithelial cells and their growth to schizonts completes the life cycle.

This typical course of development is well represented by the tabular outline given by Lühe and reproduced here. The stages connected by a single vertical line (|) are successive generations in the life cycle; those connected by the sign of equality (=) are produced by growth or metamorphosis within the single generation.

DEVELOPMENT OF EIMERIA.



This general plan of development is modified in the individual species in various manner. The most striking modification is a simplification by suppression of the entire schizogonic cycle, so that the macrogametes and microgametocytes arise directly from the sporozoites which have penetrated epithelial cells.

The coccidia parasitize almost all groups of the animal kingdom, and are distributed over the entire world, although, as might be expected, the majority of reports thus far made concerning their presence come from European countries.

For the subdivision of the group Léger's proposal to use the number and form of the sporocysts and of the sporozoites has been generally adopted. The adjoined table gives a review of the common genera arranged according to Léger's scheme.

Ripe oocyst contains	Numerous sporozoites	No sporocysts. ASPOROCYSTIDEA	Legerella.
		Many sporocysts each with ..... POLYSPOROCYSTIDEA.	One sporozoite ..... Barroussia.
			Two sporozoites ..... Adelea.
			Three sporozoites ..... Eucoccidium.
			Four sporozoites ..... Klossia.
	Eight sporozoites	Two sporocysts each with four sporozoites. DISPOROCYSTIDEA	Isospora.
	Four sporozoites	Four sporocysts each with two sporozoites. TETRASPOROCYSTIDEA	Eimeria.
		Two sporocysts each with two sporozoites	Cyclospora.

Some confusion has prevailed regarding the correct names of the various genera. The original cause of this difficulty rests on the fact that the two phases of the life cycle, schizogony and sporogony, were discovered and named separately, and that their relations as parts of the development of a single species did not become known until a much later date. All of the human parasites thus far recorded from this group fall within the limits of a genus named *Coccidium* by R. Leuckart in 1879, and this name has been generally incorporated into works on the subject. At a very recent date, however, Stiles and Lühe have independently called attention to the fact that the name *Eimeria*, introduced in 1875 by Aimé Schneider, has the right of priority, and must replace the more common form according to laws of zoological nomenclature. This is really fortunate from the general standpoint since the name coccidia has been very generally used for the entire group as well as heretofore for the genus; yet this is not in the interest of precision, and may evidently lead to serious misunderstanding. Henceforth the name coccidia can be used only in the more general sense.

The genus *Eimeria* is the best known of all. Its most important characteristic is the formation in each oocyst of four sporocysts, each with two sporozoites. A residual mass of protoplasm is always present in the sporocyst with the sporozoites, and a similar residual mass is sometimes formed in the oocyst with the growth of the sporoblasts. Of the many species assigned to this genus, the most important and better known forms which are pathologic to man and some domestic animals are included in the following key:

1. Oocyst with residual mass..... 2
1. Oocyst without residual mass..... 3
2. Oocyst oval, 33–49 μ by 16–28 μ; sporocyst spindle-shaped (rabbit, man).....*E. Stiedæ* (Lind.)
2. Oocyst spherical or cylindrical, 15–32 μ by 11–17 μ; sporocyst oval (mouse).....*E. falciformis* (Schuberg)
3. Simple forms. Oocyst oval to cylindrical, 24–35 μ by 13–20 μ. .....*E. hominis* (Riv.)
3. Twin forms.....*E. bigemina* (Stiles)

Eimeria Stiedæ (Lindemann 1865).—(Syn.: *Monocystis Stiedæ* Lindemann 1865; *Psorospermium cuniculi* Rivolta 1878; *Coccidium oviforme* Leuckart 1879; *C. cuniculi* Raillet 1893; *Pfeifferia princeps* Labbé 1896; *Pfeifferella princeps* Labbé 1899. *Eimeria cuniculi* Lühe 1902.)

All stages are known. Oocyst (Fig. 5178) in the liver of rabbit, oval 0.033–0.049 mm. long, 0.015–0.028 mm. broad. Cyst wall heavy, smooth, with opening at one pole. The coarsely granular protoplasm completely fills the cyst, but later contracts to a spherical mass at the centre (0.017 mm. in diameter). Spore formation outside the host requires two to three weeks. The entire sphere divides into four sporocysts each with a thick covering and with a length of 0.012 to 0.015 mm. and a breadth of 0.007 mm. Two comma-shaped sporozoites are formed in each sporocyst, and a granular residual mass of protoplasm lies in the hollow between their enlarged ends (Fig. 5179). The sporozoites are set free by gastric digestion. They ascend the gall ducts, pene-

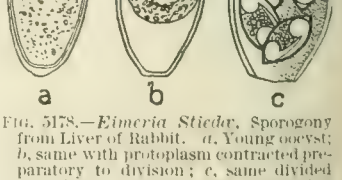


FIG. 5178.—*Eimeria Stiedæ*. Sporogony from Liver of Rabbit. *a*, Young oocyst; *b*, same with protoplasm contracted preparatory to division; *c*, same divided into four sporocytes, each containing two sporozoites which have already developed. Magnified. (*a*, *b*, after Leuckart; *c*, after Simond.)

trate the epithelial cells, and when fully grown measure 0.02–0.05 mm. in length by 0.02–0.039 mm. breadth. They divide into from 30 to 200 merozoites (Fig. 5176) which spread the infection. Ultimately the formation of macro- and microgametes leads to the fertilized sporont stage, the oocyst.

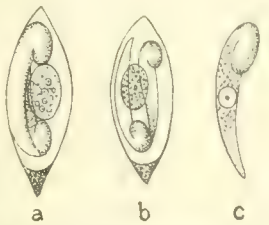


Fig. 5179.—*Eimeria Stiedæ*. *a*, *b*, Sporocysts each with two sporozoites and residual mass; *c*, a single sporozoite. Highly magnified. (From Railliet, after Balbiani.)

This species is an abundant parasite of the rabbit, in which it parasitizes in the epithelium of gall ducts and liver. According to the degree of infection sooner or later inflammation and proliferation of the epithelium lead to the formation of nodules of caseous matter, containing amid various remnants coccidia in all stages of development. These conditions may lead to severe sickness or even to the death of the host; in other cases the animal recovers as the process of schizogony appears to have distinct self-limitations. The infection is spread by the contamination of food with spore-infected fæces.

Several cases of human infection are on record. Evidently conditions favor such infection only rarely. To

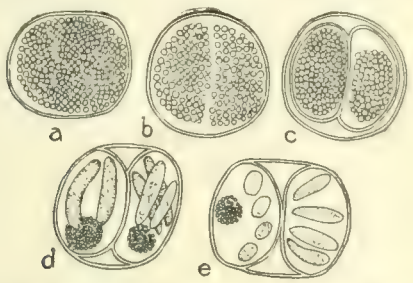


Fig. 5180. *Eimeria bigemina*, Sporogony. *a*, *b*, *c*, Division into two masses; *d*, *e*, formation of sporoblasts with residual mass. Highly magnified. (After Stiles.)

the four positive cases cited by Leuckart, all in Germany and Austria, Silcock has added another from London. A number of doubtful cases are also included here by some authorities. The observations of Thomas in Boston, according to which this species was found in a small cerebral tumor surrounded by bone tissue, has little to support the diagnosis in view of the normal condition of the liver and intestine, and has been universally questioned by reviewers. In any event the supposed coccidia cannot belong to this species, or any other yet reported from man, on account of their size (0.014–0.022 mm. in length). They correspond, however, in size nearly to the coccidia reported by Stiles from sheep which belong to a species as yet unnamed. More probably they are not coccidia at all.

Eimeria hominis (Riv. 1878), nec. R. Blanchard 1895.—[Syn.: *Cytospermium hominis* Rivolta 1878; *Coccidium perforans* R. Leuckart 1879; *C. hominis* Railliet 1893; *Pfeifferella princeps* (Labbé 1899) in part.]

Oocyst (Fig. 5177) 0.024–0.026, or even 0.035 mm. long by 0.0128–0.014 or even 0.02 mm. broad, plumper than those of *E. Stiedæ*, from which also they differ in the constant presence in sporulation of a residual mass of protoplasm that is said to be constantly absent in the latter species. (Compare Figs. 5177 and 5178.) Here also only three to four days are necessary to bring the division of the contents of the oocyst into sporoblasts (sporocysts).

This species, which is so closely related to *E. Stiedæ* that many authors regard them as identical, parasitizes in the intestinal epithelium of the rabbit, where it evokes serious, often fatal epidemics. Railliet and Lucet have demonstrated that infection takes place by the ingestion of ripe spores, and rapid schizogony brings about in a few days serious auto-infection involving the epithelium and Lieberkühn's glands so as to occlude the latter. The forms found in horse, goat, cattle, sheep, pig, and other wild species are usually regarded as varieties, but the considerable differences in form and size make it more probable that some at least represent distinct species.

Eimer found in two bodies examined in Berlin the epithelium of the intestine filled with coccidia, and even in large part destroyed by them. These are probably referable to this species. Other authors have reported the discovery of coccidia in human fæces at various times without furnishing data for the determination of the species concerned.

Eimeria bigemina (Stiles 1891).—(Syn.: *Cytospermium villorum intestinalium canis et felis* Rivolta 1874; *Coccidium bigeminum* Stiles 1891.)

Oocyst (Fig. 5180) 0.012–0.015 mm. by 0.007–0.01 mm. (in dog), or 0.008–0.01 mm. by 0.007–0.009 mm. (in cat), or 0.008–0.012 by 0.006–0.008 mm. (in polecat). The oocyst divides into two parts, each of which encysts and forms four sporocysts. The oocysts occur not in the epithelium, but in the central tissue of intestinal villi (Fig. 5181).

The species was first seen as early as 1854 by Fink, who, however, misinterpreted the character of the objects. It has often been confused with *E. hominis*, from which the above characteristics easily distinguish it. A case of human infection, published by Virchow in 1860, and another by Grunow in 1901, very probably belong here. The description given by Railliet and Lucet of coccidia discovered in the fæces of a mother and child who had long suffered from chronic diarrhœa corresponds well with this species in the small size of the bodies found, and is also probably referable to it. The form is evidently only an occasional parasite of man, and infection probably results from lack of cleanliness or too intimate association with pet dogs or cats. It may be that the forms discussed as varieties from different hosts actually represent different species. Stiles has found this species in dogs killed in Washington, D. C.

It is not surprising in view of the imperfect acquaintance with this group that all sorts of questionable structures should be referred to it. They are all such as have been reported from man usually in connection with some abnormal condition, and frequently also on the basis of a single occurrence. In most cases only scanty data are given concerning the supposed coccidia, and even of the best known of these problematic structures too little can be said to determine their true nature or position in the zoölogical scheme. It is best to call attention to certain of these cases briefly, in order that if possible further data should be accumulated to elucidate their real character. Perhaps the most sporozoon-like of all are bodies described by Rixford and Gilchrist from two cases studied at the Johns Hopkins Hospital in 1897; their characters so far as known do not easily permit of their classification in the coccidia (s. str.).

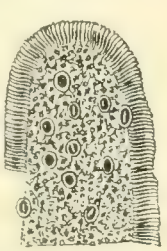


Fig. 5181. *Eimeria bigemina* in Transsection of Villus from Intestine of Dog. Highly magnified. (After Stiles.)

Coccidioides immitis Rixford and Gilchrist 1897.—(Syn.: *C. pyogenes* Rixford and Gilchrist 1897.)

Unicellular spherical bodies from 0.007 to 0.035 mm. in diameter.* So-called capsule thick, doubly contoured, enclosing a finely granular protoplasm with a clear zone [ectosarc?], 0.002–0.003 mm. wide, between capsule [pellicle?] and contents. No vacuoles seen; nucleus not demonstrated. Position of parasites usually intracellular, sometimes, however, extracellular. Sporozoites [merozoites?] ap-

* The authors give the size of the adult (p. 229) as 15 to 27 μ; again in the diagnosis (p. 243) as 16 to 30 μ, and finally in their summary (p. 246) as 7 to 27 μ. In the second case the parasites are given as 20 to 35 μ in diameter

proximately one hundred in a capsule, 0.001–0.002 mm. long.

Found primarily (?) in the skin, later generally throughout internal organs also. Reported from California and Buenos Ayres. All cases reported concern males of thirty to forty years of age.

In the first case the disease first appeared on the back of the neck and spread very slowly, causing death in

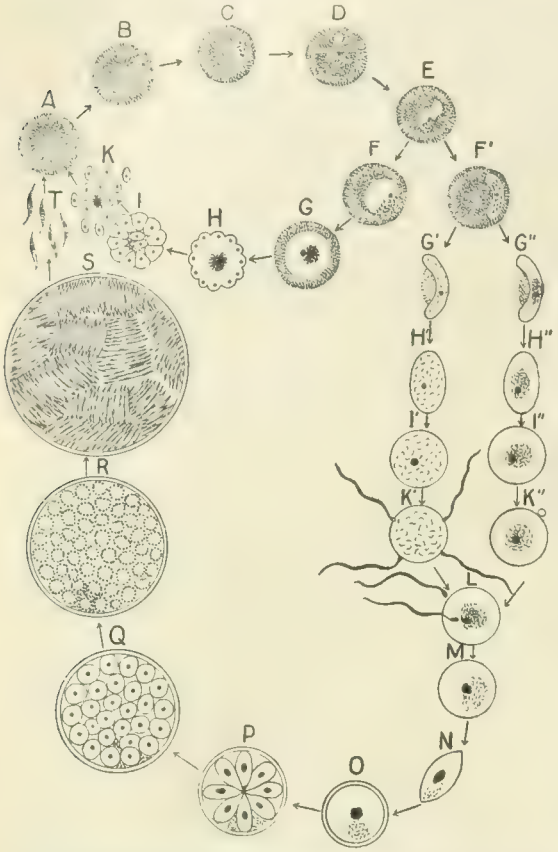


FIG. 5182. Development of *Plasmodium immaculatum*. *A*, *E*, *G*, *K*, Schizogony in human blood; *F'*, *L*, formation of gametes and fusion of same; *M*, *N*, *T*, sporogony in mosquito. Somewhat diagrammatic. For further details see text. (After Neveu-Lemaire.)

about ten years. It was only very slightly contagious, if at all, as beyond the original sores new lesions appeared only in two spots on the patient's body, and none of those who came in contact with him are known to have become infected. Some inoculation experiments were successful, but no cultures. The cutaneous lesions resembled tuberculosis cutis in character, being the seat of genuine caseation or coagulative necrosis. Both to the naked eye and microscopically the nodules were indistinguishable from tubercles save that they contained the protozoa and did not contain tubercle bacilli. In the opinion of the discoverers this seems to indicate the power to produce toxic products which possess pyogenic properties, causing both the local lesions and general symptoms. From the fact that the whole alimentary canal and mesenteric glands remained normal throughout the course of the disease, the authors exclude the supposition that the parasites entered the system through the digestive tract. The parasites were particularly abundant in the caseous foci, and occurred in far greater numbers in the lesions of the internal organs than in the cutaneous lesions. Often these parasites were found in multitudes in giant cells. They were searched for in vain only in the membranes and substance of the brain.

Another case was reported by the same authors, and like the first occurred in a native of the Azores, who had been resident in California for a number of years. The disease was acute rather than chronic as in the first; and was very destructive as the patient lost both eyes, the nose, and much of the lip, and one ear in the course of three months. According to the authors the parasite was a different species, but the distinctions are insufficient to warrant a separation of the two in our present state of knowledge. The authors identify with their cases a third, reported by Wernicke in 1892 from Buenos Ayres. Wernicke gave only an incomplete description of the parasite, and regarded the cutaneous affection as a mycosis fungoides. The protozoa he found measured from 7 to 30 μ in diameter.

There are other reports of less definiteness than those just considered, and some of the questionable structures noted therein have found an explanation within recent times. Thus the psorospermcysts of Lubarsch and Ribbert, which were supposed to play a part in diseases of the urinary passages, are in reality metamorphosed nests of epithelial cells normally found in the urethra. The structures found by Künstler and Pitres in pleural exudate and interpreted by Blanchard as a sporozoon, *Eimeria hominis* R. Blanchard 1895, I have preferred to interpret as *Echinorhynchus* eggs (*Cf. Nematoda*, page 225). More uncertain still are Severi's "monocystic gregarines" from the lung parenchym of a still-born child. They are described as oval in form, exceedingly variable in size (0.003–0.03 by 0.0015–0.015 mm.), covered by a thin membrane, and either free or in epithelial cells; it is difficult to interpret them in any satisfactory manner. Some of these doubtful structures are discussed as appendices to the next sub-order, the Hæmosporidia, to which they show a certain similarity.

An error of the reverse type is that frequently made in the past of diagnosing eggs of parasites as coccidia. Thus nematode eggs have once been reported as coccidia, and eggs of trematodes many times. Were it not for the extremely small size of the structures described, the case of J. J. Thomas, noted above, concerning coccidia in a brain tumor would find its easy explanation in this same manner.

The Hæmosporidia, like the Coccidia, are characteristic cell parasites. The period of schizogony or multiplicative reproduction is passed in the blood cells, and only very exceptionally in the cells of other organs. These stages have long been known, and with them a few preparatory stages to the sporogonic cycle, although the latter have been entirely incorrectly interpreted as degenerative changes, etc. So far as is known this sporogonic cycle takes place only in the body of another host; and for the Hæmosporidia of mammals and birds this host is a blood-sucking insect in which the process of sporogony is carried out in the wall of the alimentary canal, and the sporozoites collect in the salivary glands, whence they are injected by the act of biting into a new host to start anew the schizogonic cycle. The close relationship of these forms to coccidia is evident from a study of the life history, as Doflein indicates most aptly in calling them coccidia adapted to parasitism in the blood system.

The life history may be outlined from that of the æstivo-autumnal parasite (Fig. 5182). The earliest stage of the parasite which occurs in the erythrocytes is a minute amœboid body (*A*) which increases rapidly in size, manifesting considerable amœboid activity (*B–E*). In connection with the growth of the organism particles of a black pigment matter, named melanin, are stored up in its protoplasm (*F*, *G*). The nucleus of the parasite, at first single, begins to divide rapidly when the organism has reached its maximum size and the daughter nuclei collect about the rim of the organism (*H*). Radial lines of division appear in the protoplasm (*I*), and the whole falls into a group of young germs or merozoites (*K*) about a central residual mass of protoplasm loaded with the pigment already referred to. The merozoites infect new blood cells, and the process of schizogony is repeated until conditions, as yet unknown, bring in a new set of changes,

the starting-point of another cycle, the sexual phase, or sporogony.

The merozoites develop to individuals differently formed from the schizonts and of two sorts, the one finely granular and opaque (*G*), the other hyaline in appearance with a few conspicuous pigment granules (*G'*). These forms are shaped like a bean in the species under consideration, and are those previously designated as half-moon or crescentic bodies. When fully grown they desert the corpuscle (*H*, *H'*) assume a spherical form (*I*, *I'*). The macrogamete extrudes a portion of the nuclear substance (*K'*) and is mature. The nucleus of the microgametocyte divides, the parts migrate to the surface and form microgametes by a small accumulation of plasma about each (*K'*), leaving a large central residual mass. These two gametes copulate, their nuclei fuse, and the product (*M*) is the starting-point of the sporogonic cycle, the sporont.

The changes leading to the perfection of the sexual cells take place only after the blood has been drawn into the stomach of the new host, the blood-sucking insect. Abnormal stimuli may, however, bring about some of the changes, as in cultures of malarial blood. The copula acquires an amœboid form (*N*) necessary for its attainment of a location within the tissue of the new host. This motile stage, which has been denominated the ookinet, is a gregarine-like organism, and penetrates an epithelial cell, where it transforms itself into an immobile spherical oocyst (*O*). After nuclear division there are formed in the oocyst numerous sporoblasts (*P*, *Q*), which, however, never acquire a heavy membrane, *i.e.*, never become sporocysts as in the coccidia. Each sporoblast gives rise to a large number of sporozoites (*R*, *S*), which are set free into the body cavity of the insect host by the rupture of the wall of the oocyst. They collect as the result of an evident chemotactic influence in the salivary gland, and are injected into a new host when the insect bites. There they enter the erythrocytes and the life cycle begins anew.

The organisms included in this sub-order are the cause of serious diseases, and their number is being rapidly increased by the investigations of most recent times. Many doubtful forms have also been placed temporarily under this heading, so that it is impossible to give a synopsis of the genera, or to fix the precise limits of the sub-order itself.

Most prominent of the forms which are included here are the parasites of human malaria. Grassi still regards these all as merely varieties of one species. This is clearly doing violence to the ordinary zoological significance of the word. On the other hand, several investigators have grouped them into two genera, a plan which I myself followed in an earlier paper. Here they will be treated as three species of one genus in accord with a recently expressed view of Schaudinn, and with the known facts regarding their clinical manifestations, structural differences, and life histories.

The genus *Plasmodium* includes in addition to these species the parasite of avian malaria also. It was established in 1885 by Marchiafava and Celli, and although the name is employed here in a sense utterly at variance with its meaning as a term in general scientific use, yet the rules of zoological nomenclature call for its retention. The malarial organism was first seen and figured by Kleucke in 1843 without any idea of the significance of the structures viewed. Laveran in 1880 was the first to attach etiologic significance to the structures he described from the erythrocytes in cases of malaria. A large number of investigators participated in the gradual elucidation of the schizogony of these parasites. It was 1896, however, before Manson set forth distinctly the agency of the mosquito in transmitting the disease. Just a year later Ross actually followed for the first time the fate of the parasites of avian malaria in the mosquito's stomach, and their development up to the infection of a new host by the sporozoites. Ross' observations on avian malaria were confirmed soon after by Grassi and other Italian investigators for human species of the malarial parasite.

The complicated terminology in this group, due to the continual changes introduced by various investigators, renders it advisable to give here for general information the table prepared with such success by Lühe, which shows the correspondence in the nomenclature of the chief investigators of recent date. The terminology of Schaudinn, which is followed in this article, has been more generally adopted than any other, and has much in favor of it from every standpoint. (See table below.)

The extensive consideration which the subject has received in previous articles in the REFERENCE HANDBOOK (compare *Malaria, Mosquito in Relation to Human Pathology, Plasmodium Malariæ*) renders it necessary here only to insert a brief diagnosis of the three species, and refer to the articles noted for further details.

Plasmodium malariæ (Laveran 1884). (Syn. *Oscillaria malariæ* Laveran 1881. *Plasmodium* var. *quartana* Golgi

Schaudinn, 1899 and Lühe, 1900.	Ross, 1898.	Ross, 1899 and 1900.	Ray Lankester, 1900.	Harvey Gibson, 1900.	Koch, 1899.	Grassi, 1898 1899.	Grassi, 1900.
Schizogony.					Endogenous development.	Sporulation (fase asporulare).	Monogonia (generazione neutrale) per sporogonia conitomica.
Schizont	Sporulating form.	sporocyst (young form amœbula s. myxopod).	Oudeterospore . .	...	Full-grown parasite.	Amœboid form.	Mononte.
Merozoite .		spore; becomes later after entrance into erythrocyte amœbula (s. myxopod).	Nomospore ...		Theilungskörper.	1898: amœbula .. 1899: sporozoite.	Sporozoito (monogonico).
Macrogamete		Macrogamete (female gametocyte; young form: amœbula s. myxopod).	Gynospore .	Ovum.	Female parasite	Macrogamete s. ooid.	Makrospore.
Microgametocyte.	Flagellated body.	Male gametocyte (young form: amœbula s. myxopod)	.....		Male parasite ..	1899 [illegible] togen.	Anfizoito [illegible] gameti.
Microgamete ..	Flagellum..	Microgamete	Androspore ...	Sperm ...	Spermatozoon..	Mikrogamet s. spermoid.	Microspora
Ookinete (copula spotoni) .	Vermicule ..	Zygote	Gametospore	Oosperm	Wurmchen ..	1899: zygote	Vermicolo
Oocyst (copula spotoni).	Coccidium..	Zygote	Gametospore ..	Oosperm	Coccidienanlage	1899: zygote .	amfionte.
Sporoblast		1899: zygotomere... 1900: mere, becomes blastophore.					Masse cloroplasmatiche più o meno poligonale.
Sporozoite	Germinal rod.	1899: zygotoblast .... 1900: blast.	Gametoblast s. gametoclast s. filiform young	Zooid ...	Sichelkeim .	1899: spore . . . 1899: sporozoite....	Sporozoito (amfigonico) Young form: sporoblasto s. sporozoitoblasto.
Sporogony.....		.....	.....	.....	Exogenous development.	Exogenous development.	Amfigonia (generazione sessuale) per sporogonia conitomica.

1890; *Hæmamœba malariæ* Grassi et Feletti 1892; *H. Laverani* var. *quartana* Labbé 1894; *Pl. malaria quartanum* Labbe 1899.)

Young form in erythrocyte small, unpigmented; movement slow; pigment in coarse granules, first visible in about twenty-four hours, and peripheral in position. Movement decreasing until in sixty hours after the attack, or twelve hours before the next, the spherical *Plasmodia* fill almost the entire corpuscle. Having reached a diameter of about 0.007 mm. schizogony begins, and nine to twelve (rarely six or fourteen) merozoites are formed which are very regular (Fig. 5183, *e*). The melanin granules move in radial lines and collect in the central residual mass, from which the merozoites separate themselves in seventy-two hours. The synchronous release of these germs brings another paroxysm at this time, whence the name of quartan fever for the disease induced by this species, which is also often designated the quartan parasite. The gametes are few in number, spherical, and characterized by active streaming in the protoplasm. The sporogony of this species in *Anopheles* goes on at a minimum of 16.5° C., and stops before the maximum of 30° C. is reached. *Plasmodium malariæ* is found farther north than either of the other human malarial parasites, but does not extend into the tropics.

FIG. 5183. *Plasmodium malariæ*, Schizogony. *a*, *b*, Growth of schizont; *c*, nuclear division; *d*, formation of merozoites; *e*, release of same by destruction of erythrocyte, residual mass at upper side of group. Magnified. (After Bastianelli and Bignami.)

Plasmodium vivax (Grassi et Feletti).—(Syn.: *Hæmamœba vivax* Gr. et Fel. 1892; *Pl.* var. *tertiana* Golgi 1889; *H. Laverani* var. *tertiana* Labbé 1894; *Pl. malaria tertianum* Labbé 1899.)

Young stages in the erythrocytes are very active. Pigment granules are fine, and light brown in color. The fully grown schizont completely fills the red corpuscle, which is usually swollen and bleached in color. This stage measures 0.008–0.01 mm. in diameter, and produces fifteen to twenty merozoites in schizogony, which requires for its completion just forty-eight hours, whence the common names of tertian fever and tertian parasite. The pigment forms a solid mass in the centre, and the merozoites form a double ring about it, or more frequently an irregular mass. Schizogony occurs preeminently in the spleen. The gametes are abundant at a certain period, of spherical form, and distinguished from

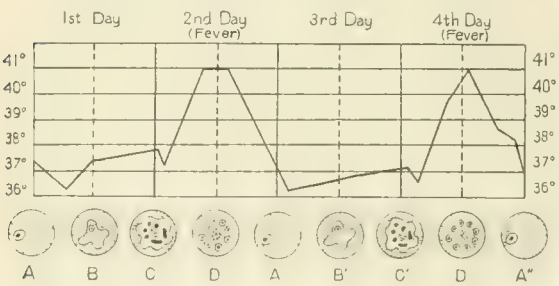


FIG. 5184.—Development of *Plasmodium vivax* in Relation to Temperature Curve of Patient. (After Dollein.)

the schizonts above all in the form of the pigment, which is in coarse granules or bacilliform masses. They reach two to three times the diameter of an erythrocyte. The sporogony in the body of *Anopheles* requires eight days at a temperature of 28°–30° C.; 17° C. is the minimum for this stage of development. This corresponds to the occurrence of the disease in the tropics and subtropics. The relation of the body temperature of the host to the development of the parasite is well shown in the accompanying diagram (Fig. 5184).

Plasmodium immaculatum (Grassi et Feletti).—(Syn.: *Laverania malariæ* Gr. et Fel. 1890; *Hæmamœba malariæ præcox* Gr. et Fel. 1892, nec. *H. præcox* Gr. et Fel. 1890. *Hæmamœba immaculata* Gr. et Fel. 1892; *Plasmodium præcox* Doflein 1901.)

This is the smallest of all human malarial organisms. Fully grown schizonts measure only 0.005 mm. in diameter. Young form very active; pigment moderate in amount, very fine in peripheral zone. The schizont may also remain unpigmented, and this form has been regarded as a separate variety. Multiple infection of an erythrocyte is not rare, and the assumption of a signet-ring form is very common. The erythrocyte shrinks during the growth of the parasite. In schizogony seven, ten, or twelve merozoites are formed, rarely twelve to fifteen, and these are small, being only 0.001–0.0015 mm. in diameter. The length of the schizogonic cycle is not well determined, as the process takes place in internal organs, especially the spleen. It is apparently irregular, though forty-eight hours seems most probable. The gametes are crescentic or reniform, and originate especially in bone marrow. Further changes have been most carefully followed in this species. In the stomach of *Anopheles* these crescents become spherical (Fig. 5185) and the microgametes are formed and set free. The fertilization is completed by the fusion of a single microgamete with a macrogamete; and the resulting motile ookinet (Fig. 5186, *a*) penetrates the wall, entering first

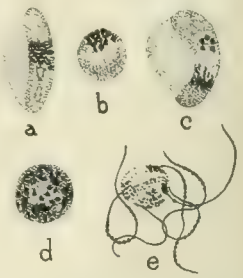


FIG. 5185.—*Plasmodium immaculatum*; Development in Stomach of *Anopheles claviger*. *a*, Macrogamete with remnant of erythrocyte; *b*, same one-half hour after ingestion by mosquito; *c*, microgametocyte with remnant of erythrocyte; *d*, same one-half hour after ingestion, the nucleus has divided several times; *e*, microgametes still attached to residual mass (so-called polymitus stage). Highly magnified. (From Braun, after Grassi.)

FIG. 5186. *Plasmodium immaculatum*. *a*, Ookinet in stomach of *Anopheles claviger* thirty-two hours after ingestion; *b*, transsection of stomach with partly developed oocysts several days later. Magnified. (From Braun, after Grassi.)

an epithelial cell and coming later to lie between the layers of the wall (Fig. 5186, *b*). The oocyst forms no special covering, but increases rapidly in size. Sporoblasts and then sporozoites are formed; the latter have a length of 0.014 mm. and a thickness of 0.001 mm., and are produced to the number of ten thousand in a single oocyst. After the rupture of the latter they accumulate in the salivary gland, lying in the secretion either within the cells or in the duct itself, whence they are expressed in the act of biting (Fig. 5187).

The sporogony requires eight days at a temperature of 28°–30° C., and 18° C. is the minimum temperature for the infection of *Anopheles*. This species gives rise to the

malarial fever designated as æstivo-autumnal, perniciosa, tropica, etc., and is epidemic only in the tropics and subtropics. This is the form which has been rated as a representative of another genus, *Laveranii malariæ*, by

FIG. 5187. Section Through Dorsal Sac of Salivary Gland from *Anopheles* with Groups of Sporozoites of *Plasmodium immaculatum* both in gland cells and in duct. Isolated sporozoite at right more highly magnified. (From Lang, after Grassi.)

many observers. While its separation from the genus *Plasmodium* is perhaps a convenience, it seems hardly justifiable on scientific grounds, as the differences between it and the other species are not of generic rank.

Uncertain Species.—According to the work of certain investigators, particularly Celli, there exists a true quotidian malarial parasite, which is related to *Plasmodium immaculatum*, although smaller and completing the schizogony in twenty-four hours. The supposed species is found in Italy particularly in summer and fall, and is regarded by most authors as at most a variety of *Pl. immaculatum*. Still other forms from tropical regions have been regarded as distinct species without sufficient evidence as yet for this opinion.

There are yet other hæmatozoa of which it may be said that their exact relationship has not been sufficiently demonstrated to give them a definite place in the system, but which in all probability will be included in this suborder, though evidently not in the same genus with the malarial organisms just described.

In this connection should be noted the parasite of the spotted fever or tick fever of the Rocky Mountains, a new disease especially virulent in the valley of the Bitter Root River in Montana, where it has been known for twenty years, but present apparently also, though in milder form, in other parts of Montana, Idaho, Wyoming, Nevada, and Eastern Oregon.

Wilson and Chowning were the first to note ovoid intracapsular bodies in stained blood preparations, and to determine that in fresh blood these bodies manifest amœboid movements. These observations have been confirmed by later investigators, and the hæmatozoon is regarded by all as probably the cause of the disease. A brief description of the organism may be given here.

The smallest forms, or the first phase of Wilson and Chowning, are intracellular, ovoid bodies and measure 0.0015-0.002 mm. in length by 0.0005 to 0.001 mm. in thickness. They resemble slightly young schizonts of malaria, and more strongly the organism of Texas fever of cattle. These bodies occasionally change position in the corpuscle, and according to Anderson project pseudopodia quite rapidly. Two such bodies may lie in a single corpuscle. In the second phase the bodies are solitary in the erythrocytes, oval, ellipsoidal or spherical in form, and from 0.002 to 0.003 mm. thick by 0.003 to 0.005 mm. long. This phase is actively amœboid with the formation of pseudopodia in various directions. The third phase is seen in pyriform bodies arranged in pairs with the pointed ends approximated, and in rare cases distinctly united by a fine thread. This form is not amœboid.

Though the parasites are not found in large numbers in the circulating blood, only a few being present in each field of a preparation of freshly drawn blood, yet in the capillaries of tissues removed at autopsies from one to five per cent. of the erythrocytes are infected. This is marked in the lung, spleen, liver, and kidney, where also are found many red cells included in phagocytes, being faintly outlined within the protoplasm of the latter, and each containing a large parasite. In tissues taken some hours after death, the organisms are almost all spheroidal. They are present in the blood at least twenty-four days after recovery.

The organism is apparently transmitted by ticks, and all cases of the disease show a history of tick bites about one week before the onset. Stiles made a provisional determination of some ticks from the region as *Dermacentor reticulatus* but in correspondence later expressed the view that certain differences though slight justify placing these forms in a new species. Some facts point to the existence of another normal mammalian host for the parasite, and the gray gopher has been indicated as the most probable form. Further study is necessary to establish the character and development of this parasite, its exact systematic position, and its positive relation to the disease. Its superficial resemblance to *Piroplasma bigeminum*, the cause of Texas fever in cattle, has already been mentioned.

Myxococcidium Parker, Beyer, Pothier 1903.—Schizogony unknown; sporogony in *Stegomyia fasciata*. Only one species, thus far imperfectly known.

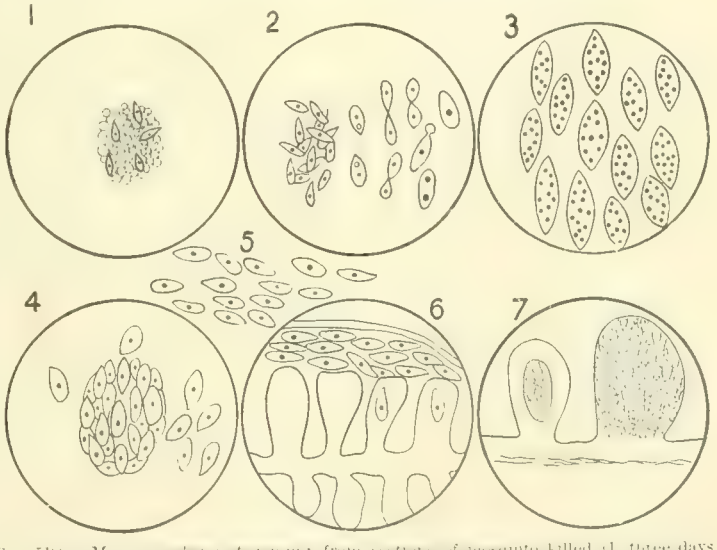


FIG. 5188. *Myxococcidium stegomyiæ* from sections of mosquito killed (1) three days, (2) four days, (3) five days, (4) six days, (5) six to twelve days, (6) twelve days, (7) fourteen days after feeding on blood of yellow-fever patient. (Unpublished sketches, by courtesy of J. C. Smith.)

Myxococcidium stegomyiæ Parker, Beyer, Pothier 1903 (Fig. 5188).—A fusiform body (ookinet?) 0.003-0.004 mm. long by 0.0015-0.002 mm. broad in lumen of stomach and œsophageal diverticulum, about three days after mosquito has bitten yellow-fever patient; this body is provided with a nucleus. A spherical body (oocyst?) in

the œsophageal diverticulum, embedded in an albuminoid mass of unknown character. This becomes mature and breaks up into numerous (thirty to forty) elongated oval bodies (sporoblasts?), 0.003 mm. long by 0.002 mm. broad, which enter the cells of the salivary gland, and then coming to rest (sporocysts), divide into numerous very minute bodies (sporozoites?).

The parasite was found in the yellow-fever mosquito (*Stegomyia fasciata*) from Vera Cruz, Mexico, by Drs. Parker, Beyer, and Pothier, Working Party No. 1, Yellow-Fever Institute of the United States, Public Health and Marine Hospital Service. According to these authors the mosquitoes used were fed on the blood of a yellow-fever patient, and with due precautions against infection from any other source were killed at stated intervals from the second to the thirtieth day. A careful study of sections of these mosquitoes in which the Working Party mentioned received valuable assistance from Mr. J. C. Smith, of New Orleans, resulted in the demonstration of the life history of the organism somewhat imperfectly as outlined above. More recently, however, Carroll has maintained that the fusiform stage is actually a wild yeast.

The Working Party also states that yellow fever was produced experimentally with mosquitoes from a case that harbored this parasite, and the parasite was found again in mosquitoes fed on this case. Furthermore they permitted this same species of mosquito to feed on a case of malarial fever of the malignant type, on normal blood, and on other nutritive materials, and in none of these mosquitoes were found the parasites described above.

From the account given it appears that there was present in these mosquitoes a parasite, the development of which bears close resemblance to that of the malarial organism in the sexual cycle (sporogony). On the analogy of the latter parasite there should also occur in this case a non-sexual cycle (schizogony) in the blood (?) of the yellow-fever patient. Yet Sternberg, Reed, Carroll, and many others have sought in vain for such an organism; nor was the Working Party more successful. The further life history of *Myxococcidium stegomyiæ* lies even beyond conjecture, and it can only be said that negative evidence raises a strong presumption in favor of its etiological relation to yellow fever.

Quite recently Councilman, Magrath, and Brinckerhoff have made known the results of studies on the organisms of vaccinia and of variola, which go far toward establishing the nature of these oft-reported and much-questioned bodies. Much is needed to confirm these reports and to elucidate further details in life history, as well as the general relationship of these bodies. They may be considered briefly here without prejudicing the results of further study on these points. Before vesicle formation in the diseases noted, small, structureless bodies (0.001–0.004 mm. in diameter) occur in vacuoles of cells in the lower layers of the dermal epithelium. With increase in size the body shows granules lying in a reticulum, and becomes irregular in form as if amœboid. No nucleus was demonstrated. Formation of small round bodies, 0.001 mm. in diameter, closes the first stage in the life cycle. Following this oval or ring-like intranuclear bodies appear. In them several vacuoles are seen grouped around a central vacuole. They enlarge and destroy the nucleus, and come to lie in a completely degenerated cell. The vacuoles become less evident, and there appear multiple circular bodies with a central dot. These bodies measure only 0.0015 mm. in diameter, and are seen with great difficulty.

The intranuclear bodies represent the second stage in the life history, which is believed to be the sexual cycle, and produce spores which are the infecting agents. In the opinion of these authors the first cycle may exist without the second, and such is the case in vaccinia.

Apparently these are the same structures seen by L. Pfeiffer, Guarnieri, and others, who were not successful in working out the life history as it now stands, although they also did not hesitate to bring them into etiological relation to smallpox. One of the most recent of these (Govini) has even described and figured both extranuclear and intranuclear bodies in vaccinia. Questionable intranuclear bodies have also been reported by several investigators for sarcoma cells in man, but there are also other parasites belonging to this group and affecting lower animals in which an intranuclear existence is well known, *e.g.*, *Eimeria salamandra* (= *Caryophagus salamandræ*), parasitic in the intestinal epithelium of one of the salamanders, and most frequently in the nucleus of the cell parasitized.

Hæmatozoa have been described by various authors as characteristic of beri-beri or kakki, an endemic form of polyneuritis particularly prevalent in Japan and the Dutch East Indies. The infectious nature of this disease seems to be generally accepted, and at different times various forms of possible pathogenic significance have been reported from the blood. The most recent of these are amœboid bodies resembling malarial parasites, which have been studied and described at length by Glogner, and especially Fajardo. The latter demonstrates their presence in the blood in peripheral as well as inner organs, and their production of pigment and formation of spores of some sort; and yet the possible confusion with malarial or other hæmatozoa and the lack of proof concerning the distinct etiological relation to beri-beri have prevented any general acceptance of the rôle assigned to the organism.

In leukæmia also Löwit claims to have discovered amœboid organisms in the leucocytes, and to have followed their development even to sporulation, *i.e.*, schizogony. (For further details see *Leukæmia*.) The parasitic nature of such structures cannot be regarded as established until they have been studied in life and not merely in preparations of fixed blood.

In dengue, an infectious disease epidemic in hot climates, and treated at length in an earlier volume (*q.v.*) good evidence has recently been furnished that the cause is a protozoön analogous to the malarial organism, and like it transmitted by the mosquito. It is an unpigmented pyriform body found in the erythrocytes though not abundantly, and is present in second and third attacks as well as in the first. The development is slow, requiring four to eight or even ten days, and in general appearance the organism suggests *Piroplasma bigeminum* of Texas fever in cattle or the organism of spotted or tick fever in man noted above. The discoverer, Graham, also found spores in the walls of the stomach and salivary glands of the mosquito, though this portion of the life history has not yet been clearly described; in one case the time required for it was, however, only forty-eight hours. In this case it is *Culex fatigans* which harbors the organism and transmits it, although other species may also be responsible. Graham has recently reported inoculation experiments, the results of which leave little doubt as to the cause of the disease and the method of transmission.

A long series of contributions concerns objects of supposed protozoan character which have been brought into etiologic connection with various pathological conditions by investigators of the most diverse type. Such are the pseudococcidia of epitheliomata, of sarcomata, of molluscum contagiosum, etc. Three views obtain as to the nature of these bodies, according to which they are blastomycetes or myxomycetes, sporozoa or other protozoa, and finally degenerative cell products. It cannot be said that their animal nature has been at all clearly demonstrated, and beyond the mere mention they have no right to consideration in this article.

In the subclass Neosporidia are included forms which in the adult condition are multinuclear, and which produce spores during the entire vegetative period. Spore formation is very characteristic. The organism forms a number of pansporoblasts, which divide again to form sporoblasts. The latter acquire a membrane and transform themselves with somewhat complicated changes into sporocysts, each of which develops within itself only a single sporozoite. Of the two orders only the

Sarcosporidia are of importance here, and they are but imperfectly known.

The Sarcosporidia possess an oval, elongate, or sacculate body (Fig. 5189), in which pansporoblasts are formed at a very early period. They parasitize at first intracellularly the muscle fibres, but by the degeneration of these come to lie in connective tissue and develop to oval or spherical bodies of considerable size. In the youngest stages yet found uninuclear spheres 0.004–0.005 mm. in diameter with relatively large nuclei (0.002–0.003 mm.) occur in the endoplasm. The protoplasm forms a frame-work between these young pansporoblasts, which increase in size with age and become also multinuclear. While at the ends of the sacculate body new pansporoblasts are continually being formed, in the older ones nearer the centre the contents divide into many finely granular pale spheres, the sporoblasts.

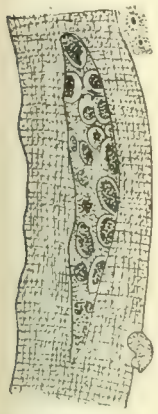


FIG. 5189.—*Sarcocystis tenella*. Longitudinal section of young stage with newly formed uninuclear pansporoblasts. Magnified. (From Wasielewski, after Bertram.)

In each of the latter is formed a single sporozoite which gradually assumes the definitive form (Fig. 5190, *a–d*). These sporozoites are usually reniform, sickle-shaped, or crescentic and very small. Some investigators claim to have discovered a polar capsule, and this has been partly confirmed by some later observers. Polar filaments are present in some cases (Fig. 5191, *b*). Theobald Smith has observed the movements of the sporozoites, and finds that in *Sarcocystis muris* there is a peculiar gliding with sudden revolutions on the long axis. This is carried out without the assistance of flagella. Smith's experiments, which were very painstaking and extended over three years, demonstrate for this species direct infection by feeding muscle tissue in which was present the parasite with ripe, mobile sporozoites. Sarcosporidia are parasitic in vertebrata, chiefly mammalia, and are common in many domestic animals.

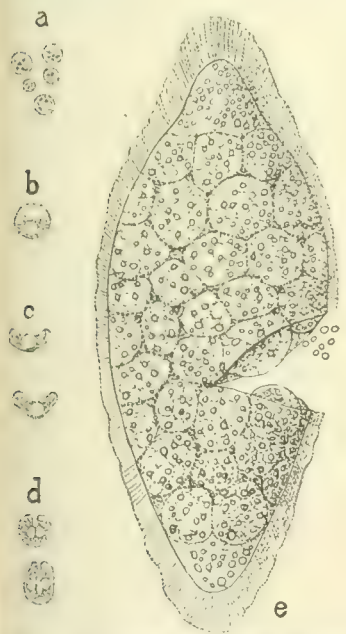


FIG. 5190. *Sarcocystis miescheriana*. *a–d*, Development of sporozoites from sporoblasts; *e*, full-grown sac, dissected out from muscle fibre, the radially striated capsule-layer on the right to show the pansporoblasts within. Magnified. (From Wasielewski, after Manz.)

Miescher in 1843 found these parasites first as cylindrical sacs in the voluntary muscles of the house mouse. Some years later Rainey found similar structures in the muscles of the pig, and the common names of these structures, often visible to the naked eye, are associated with these two investigators. The group has been but little studied, and the system is so imperfectly developed that it is advisable to omit all further mention of it, and to pass at once to a consideration of the one species which has been certainly obtained from the human body.

Sarcocystis Lindemanni (Rivolta 1878).—(Syn.: *Gregarina Lindemanni* Rivolta 1878, *Sarcocystis hominis* Rosenberg 1892; *S. Lindemanni* Labbé 1899.)

Protoplasmic body from the muscle fibres of the vocal cords, from 0.15 to 1.6 mm. long and from 0.077 to 0.17 mm. thick; membrane delicate, somewhat thickened at the ends (Fig. 5191, *a*), body distinctly chambered (Fig. 5191, *e*). Sporozoites (*d*) banana shaped, exceedingly numerous, 0.008–0.009 mm. in length.

The most certain case is that of Baraban and St. Remy, who found this form in the body of a criminal executed at Nancy. All the specimens of the parasite were in the same stage of development. The infected muscle fibres were swollen to fourfold their normal thickness. Several other uncertain cases are on record. As Theobald Smith remarks, the muscular system is not subject to the scrutiny which the viscera undergo in pathological investigations, so that the presence of these forms may be much more frequent and important than appears as yet. In the case of *S. muris* Smith has shown that the feeding of muscle tissue containing ripe mobile sporozoites to gray and white mice is followed by an invasion of the muscle fibres by the parasites, which readily become recognizable after the forty-fifth day. Nothing is known regarding the development of *S. Lindemanni*.

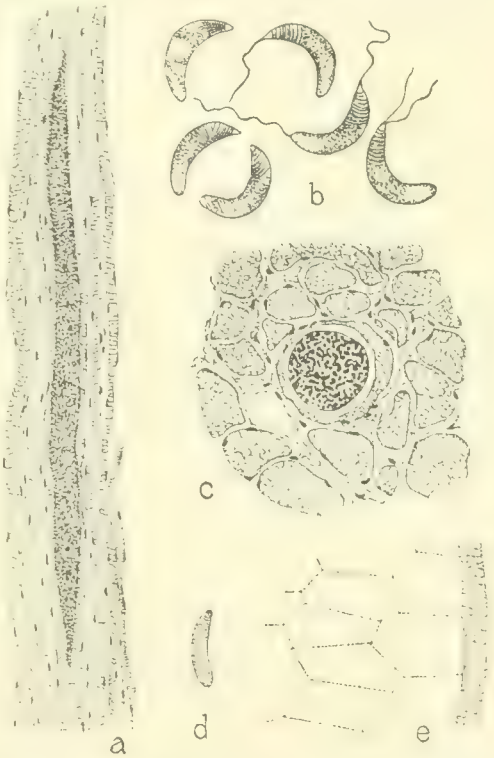


FIG. 5191.—*Sarcocystis Lindemanni* from Human Larynx (except *b*). *a*, Longitudinal section of muscle fibre with fully developed sac. × 250. *c*, Transverse section of same. × 250. *e*, Section showing chambers emptied of pansporoblasts. × 565. *d*, Sporozoite. × 1,350. *b*, Sporozoites of *S. Blanchardi* with polar filaments. × 875. (*b*, From Wasielewski, after van Ecke; other figures from Doflein, after Barbaran and St. Remy.)

The class Infusoria holds the highest rank among Protozoa, and its members are at once distinguished by the presence of peculiar organs of locomotion in the form of fine hair-like protoplasmic processes, the cilia, which are present in at least some part of the life history of all individuals in the group. By virtue of the greatly inferior length, the much larger number present on each animal, and the simple synchronous movement cilia are easily distinguished from flagella. The external zone or ectoplasm is more highly differentiated than in the forms of

Protozoa thus far considered, and the body has in consequence a more permanent form, which tends to acquire in all free species a bilaterally symmetrical structure. In the ectoplasm one finds special contractile fibrils, or myophanes, and peculiar unexplained bodies known as trichocysts. The cilia are arranged in rows, and occasionally fuse into vibrating membranes or stylet-shaped masses, cirri, in furtherance of the motor function. The firm ectoplasm forms at the mouth opening (cytostome) a groove (peristome), or a peculiar funnel-shaped pit (cytopharynx), which serves to admit food particles to the interior of the body. A differentiated anal orifice (cytopyge) is only rarely found. The contractile vacuole is always present, and often two or more occur with a more or less extended canal system branching in all directions.

One of the most striking peculiarities is found in the nuclear conditions. Typically two nuclei are present; a large somatic nucleus or macronucleus, and a small sexual nucleus or micronucleus, which usually lies close to the former. The macronucleus is always single, but there may be several micronuclei to each cell. The ordinary process of reproduction is fission or gemmation, and in this the macronucleus divides amitotically while the micronucleus undergoes indirect or mitotic division. At times one finds conjugation, or temporary and partial fusion of two individuals with the destruction of the macronuclei and of a certain portion of each micronucleus, while the remainder of each micronucleus on each side is divided equally between the two individuals. From the portions of the micronuclei fused there arise new macronuclei and micronuclei. This process has generally been looked upon as one of rejuvenation, and necessary for the continued existence and reproductive power of the individual. Certain recent investigations leave this somewhat uncertain. The complicated details of the process find, however, an evident parallel in changes connected with the fertilization of higher forms, or the union of egg and sperm cells.

Encystment is frequent, and the evident means of providing for unfavorable changes in environment, such as drought, temperature changes, etc. In parasitic forms it is related to the necessary interval of transport to a new host. In the majority of cases these protozoa are commensals rather than true parasites, and in some instances are even said to be of mutual advantage to the host, and consequently symbiotic in character. The two subclasses are distinguished on the basis of the permanence of the ciliary covering which is constantly present in the Ciliata, save during encystment, but which is found only in the young forms of the Suctoria. The latter are also supplied with peculiar sucking tubes for taking in nourishment. They do not furnish any forms found in the human body.

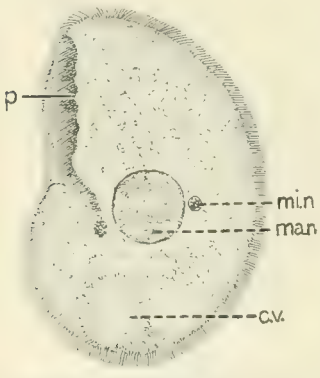


FIG. 5192.—*Nyctotherus faba*. Living. *c.v.*, Contractile vacuole; *ma.n.*, macronucleus; *mi.n.*, micronucleus; *p.* peristome. Magnified. (After Schaudinn.)

The Ciliata are present in large numbers in all fresh-water bodies, and manifest great variety of structure. They furnish many ectoparasitic species on water-living vertebrates and a few endoparasitic in higher forms, including man. The various orders into which the Ciliata are divided are based upon the number and arrangement of the cilia in the adult form. Only two of these orders call for attention here. In the Holotricha there is no spiral zone of prominent cilia or membranellæ leading to the cytostome, and the body possesses only small cilia which are more or less generally distributed. The Heterotricha have an adoral spiral zone of larger cilia, but the remainder of the body is uniformly finely ciliated.

Of the Holotricha one species has been reported from man. It belongs to the genus *Chilodon*, the distinctive features of which are included in the description of the species which follows.

Chilodon dentatus (Dujardin 1841).—(Syn.: *Loxodes dentatus* Duj. 1841; *Ch. dentatus* Guiart 1903.)

Oval, 35–55 μ long by 25–35 μ broad, flattened in ventral face, dorsal aspect strongly arched. Anteriorly a flexible membranaceous projection curved toward the left and carrying several rows of cilia on the lower aspect. Granular endoplasm confined to posterior inflated region; ectoplasm in a thin peripheral layer and forming the anterior projection. Mouth ventral, in anterior portion of the endoplasmic region, normally contracted and hardly visible, cytopharynx directed dorsally and recurved ventrad so as to form almost a complete circle. Two contractile vacuoles, macronucleus large, spherical, in posterior region.

This infusorian has been found once by Guiart, as a parasite of the human intestine in Paris, France. The animals were present in large numbers in the mucus from dysenteric stools. Care was taken to control the source of the parasite and to avoid contamination from external sources, with the result of obtaining from the dejecta on the second day after passage pure cultures of the infusorian. It is a common free-living species, and must be classed in this instance merely as an accidental parasite. Close examination of fæcal discharges will undoubtedly show the occasional occurrence of many such, especially when the resting spores happen to be abundant in the local supply of drinking-water. In this case there is nothing to show that the resting spores did not simply make the passage of the canal, and then develop almost at once in the discharges. The extreme sensitiveness of the species to changes in the environment, which has been commented upon by Guiart himself, makes this explanation of the case more probable. One should recall in this connection the record of Schaudinn, that the resting spores of a Rhizopod, *Chlamydophrys stercorea*, must make the passage of the alimentary canal in man or other animals in order to undergo development. In this case, indeed, the resting spores open in the colon and an amœboid organism emerges which does not assume the testaceous form of the adult until after the fæces are discharged from the body.

The order of the Heterotricha, already generally characterized, includes three species under two genera, which have been reported from the human host. The first belongs to the genus *Nyctotherus* Leidy 1849, which contains flattened reniform species with a peristome along the concave side from the anterior pole to the cytostome at the centre. The cytopharynx is more or less arcuate. The macronucleus is large and nearly central in location. A single contractile vacuole is present. The species of this genus occur as parasites in the alimentary canal of Anura, Myriapoda, and Insecta. A single form has been found twice in the human alimentary canal.

Nyctotherus faba Schaudinn 1899.—Body reniform, somewhat flattened dorsoventrally, left side convex, right concave and notched in the centre. Anterior end bent to the right a little, and on the right side slightly cut out; posterior end broadly rounded (Fig. 5192). Length 0.026–0.028 mm., breadth 0.016–0.018 mm., thickness 0.01–0.012 mm. Peristome a narrow longitudinal slit just at right margin of body, extending from near anterior end to middle of body. Cytopharynx tubular, short, and without guide spine at entrance. Cilia very fine and delicate as well as short. Ectoplasm thin, endoplasm granular, alveolar and without food vacuoles. Contractile vacuole large, located left of middle, near posterior end, emptying through the special anal tube. Macronucleus spherical, 0.006–0.007 mm. in diameter, with chromatin in four or five solid masses near periphery, leaving the intervals filled by a non-staining linin network. Micronucleus 0.001–0.0015 mm. in

diameter, spherical or oval, ordinarily next the macronucleus. Fission and conjugation were not observed. Encysted form oval, easily recognized by the strange macronucleus.

This species has been found only once in Berlin in a patient suffering alternately from diarrhœa and constipation. It occurred in large numbers in the fæces taken direct from the intestine, and was accompanied by *Balantidium minutum* and eggs of *Anguillula* (?) and *Anchylostoma*. The species has an especial interest here since the German physicians suggest from the history of the case that the infection may well have been attained in the United States, where the patient had lived for some time previously. A pathogenic rôle has not been attributed to the species.

Stiles reports in recent correspondence that he has encountered several cases of ciliate infection which could not be identified and at the time more exact study was impracticable. The attention of physicians should be directed more carefully to this group of organisms.

The genus *Balantidium* includes species of oval or ellipsoidal form, circular in transsection, with the anterior end somewhat tapering. The peristome has the form of a flattened funnel with the cytostome at its base. Two contractile vacuoles on the right side, sometimes two others on the left. Cytopyge terminal; macronucleus oval or reniform. The five known species are parasitic in the alimentary canal of man (two species), pig (one species), and amphibia, and in the body cavity of polychætous annelids. For the distinction of the human parasites a key to all five species is necessary. That given here is taken from Schaudinn.

1. Peristome extends to equator of body or further, cytopharynx present 2
   Peristome much shorter, cytopharynx wanting 3
2. Four contractile vacuoles, macronucleus reniform, cyst spherical ..... *B. entozoon* Clap. and Lachm.
   One contractile vacuole, macronucleus spherical, cyst oval ..... *B. minutum* Schaudinn
3. Two contractile vacuoles 4
   One contractile vacuole macronucleus oval, cyst spherical ..... *B. duodeni* Stein
4. Body elongated, spindle-shaped, or cylindrical, *B. elongatum* Stein
   Body oval ..... *B. coli* Stein

Balantidium coli (Malmsten 1857).—(Syn.: *Paramæcium coli* Malmsten 1857; *B. coli* Stein 1867.)

Form oval, slightly truncated anteriorly with very short infundibuliform peristome which lies just to the right of the anterior tip and leads to a short cytopharynx (Fig. 5193). Body 0.07–0.1 mm. long by 0.05–0.07 mm. broad. Ectoplasm and endoplasm distinct; latter with drops of oil and mucus, and according to some observers red and white corpuscles from the host. Macronucleus bean-shaped or reniform, with the small spherical micronucleus adjacent to it. Two contractile vacuoles located on the right side, but no permanent cytopyge. Fission of the free form has been observed. Conjugation has also been seen. Cysts are spherical and possessed of impervious membrane.

This species inhabits the colon of man and the pig. In the latter it occurs also in the rectum and cæcum, and is present regularly in large numbers. The pig may be regarded as the normal host, and in it this species excites no abnormal symptoms. The encysted forms evacuated with fæces are supposed to bring about the transfer of the species all the more easily that the pig is coprophagous; and yet experimental infection has been unsuccessful even in the pig. Grassi and Calandruccio have demonstrated that experimental infection of man is not successful in the case of healthy individuals. The occasional introduction of encysted forms may, however, bring about successful colonization of the canal whenever any pathologic conditions exist in the colon, although Grassi and Calandruccio argue from the slight difference in size and the failure of their experiments that the forms found in man are not of the same species as those from the pig. These conclusions do not seem to have found even limited acceptance.

Malmsten discovered *Balantidium coli* in 1857 in a man who had recovered from an attack of cholera two years before, but had since suffered from diarrhœa. The parasites were abundant in the bloody discharge of a rectal abscess, and even after its disappearance persisted in the fæces, from which they finally disappeared as a result of the use of acid enemata. In the necropsy of a subsequent case the exact seat of the parasite was determined as the anterior region of the large intestine.

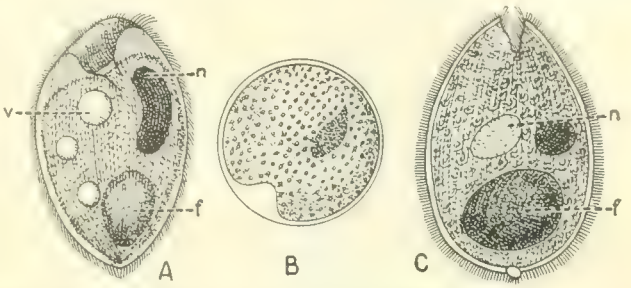


FIG. 5193. *Balantidium coli*. *A*, *C*, Free; *B*, encysted; *n*, macronucleus; *v*, contractile vacuole; *f*, food mass. Magnified. (*A*, After Leuckart; *B*, *C*, from Braun, after Casagrandi and Barbagallo.)

Many cases have been reported from man since then. Shegalow lists sixty-three in all from Russia, Germany, Scandinavia, Finland, Italy, Cochin China, Sunda Islands, and the United States of America. Strong and Musgrave have added the Philippines to this list. While this parasite has been observed regularly in obstinate diarrhœa, its disappearance is not accompanied with the cessation of the symptoms in all cases, and Balantidia have been found after the diarrhœa has stopped. The earlier idea that these protozoa were the exciting cause of the intestinal disturbances has accordingly given way in part to a view that these protozoa continue and extend the diseased condition, but are not sufficient to cause it. Some authors report, however, that the species penetrates the intestinal wall and causes abscesses in the deeper layers. Solowjev claimed even to have demonstrated them in the blood and lymph vessels of the intestinal wall. This has recently been confirmed by Strong and Musgrave.

These authors, together with several other very recent contributors to this subject, contend very strongly in favor of the pathologic rôle played by the parasite. In most post-mortems lesions have been found similar to those of amœbic dysentery. Brooks found in apes in New York extensive ulcerations in the cæcum, irregular in contour with undermined borders. The mucous and submucous coats were destroyed and the parasites were present in great numbers in the ulcerations, especially on the floor and along the sides. They even pass beyond the limits of the ulcers, apparently following the course of the lymphatic and blood-vessels. It was surmised that the parasites entered the submucosa from the crypts of Lieberkühn, in the depths of which they were often found. The Balantidia were found in the diarrhœtic stools, but disappeared with recovery of the host. But relapses were frequent, and each time the parasites reappeared in the fæces. This is explicable on the basis of their position deep in the glands of the intestinal wall, and emphasizes the difficulty of completely destroying them and preventing a recurrence of the disease.

It is difficult to avoid the conclusion that positive proof of the etiologic significance of these forms is given by the presence of abundant parasites in the lesions and in the tissues in advance of the pathologic changes, and also by their occurrence in the depths of glands and in the submucosa before the start of such lesions at these points. The opponents of this view regard the rôle of the pro-

tozoa as secondary, and look upon bacteria as primarily responsible for the lesions. This species is known to occur abundantly in some parts of this country as a parasite of the pig, and its more frequent presence in the human host than records hitherto made would show may easily be disclosed by more careful examination. It should be noted that many of the cases already on record come from the country where the chances of accidental infection are naturally greater. It is there accordingly that one should look for evidence of more extended infection of the human host. Lack of records in the past may well be due to lack of precise examination among the very cases in which the parasite is most likely to occur.

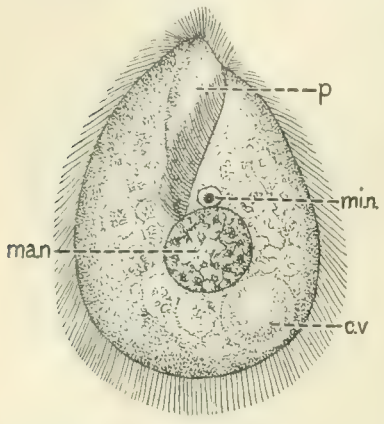


FIG. 5194.—*Balantidium minutum*, Living. Abbreviations as before. Magnified. (After Schaudinn.)

Balantidium minutum Schaudinn 1899.—(Syn.: *Colopoda cucullus* Schulz 1899.)

Body compressed pyriform or oval (Fig. 5194). Length 0.02–0.032 mm.; breadth 0.014–0.02 mm., or in the ratio 3:2. Anterior end bluntly pointed, often slightly twisted dextrad or sinistrad. Posterior end broadly rounded. Peristome a slender cleft, broader anteriorly, pointed posteriorly and deeper; extending from near anterior tip to centre of body; in the living animal continually opening and closing; left margin with hyaline membrane. Adoral cilia heavier and longer than those of the body generally, only on the left peristome margin beneath the membrane. Body cilia long (0.007–0.008 mm.) slender. Hyaline ectoplasm thin, distinct from granular endoplasm, which contains many vacuoles. These are filled with fine granules, and large food masses or excretory crystals are not present. Contractile vacuole single, near posterior end on left side. No permanent cytopyge. Macronucleus spherical 0.006–0.007 mm. in diameter; centrally located. Micronucleus single, anterior to macronucleus at its surface, 0.001 mm. in diameter. Division occurs, but conjugation has not been observed. Cyst oval.

Reported twice, once in company with *Nyctotherus faba* (*q. v.*) and once in Berlin also without that species. In both cases this form was abundant during the diarrhœa, but with the exception of a few cysts, disappeared as soon as the stools became firmer. Purgatives brought the infusorians again in numbers into the stools. This condition indicates that they inhabit the small intestine, perhaps the duodenum, rather than the colon, and make their appearance when carried outward by more fluid contents and rapid passage of the canal. As other species of the genus are harmless commensals in the canal of Amphibia, this species is probably not pathogenic. It should be kept in mind that confusion of *B. coli* and *B. minutum* may occur if the examination is not made with precision, and perhaps some cases of the former, already on record, actually concern the latter species.

As pseudo-infusoria may be designated a long series of structures reported from various sources, and often the object of repeated discovery by those unfamiliar with the field. Thus in mucus or sputum in case of affection of the air passages, bodies moved by cilia have been interpreted as genuine parasites and assigned an etiological rôle in the disease. In contravention of this view may be urged the variable and irregular form of such bodies, their rapid and special degeneration and their source, which amply demonstrate their origin as detached ciliated cells from bronchi, trachea, or nasal cavity. Such bodies are the asthma parasites of Salisbury, and the protozoa of whooping-cough described by Deichler and Kurloff.

Much less worthy of serious attention are the reports of various writers, especially Lindner, that certain forms, well known as free-living species, namely, unstalked vorticellids, are the cause of various gastric disturbances in man and certain domestic animals. The statement of Schaudinn, that he has found repeatedly active vorticellids in fresh fæces, but only after water enemata, is sufficient indication of the means by which such marvellous discoveries as those of Lindner and others are achieved. Quite recently I was asked to examine a slide containing organisms from fresh urine, and these were not echinococcus bladders as diagnosed, but unmistakably free living forms, and probably contracted rotifers whose presence was due to the contamination of the vessel, or possibly of the sample of urine examined.

Henry B. Ward.

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ADDENDUM.

"PROTOZOA IN SCARLET FEVER?*—In four cases of scarlet fever, which came to autopsy at the Boston City Hospital, there was found a series of bodies which strongly suggest the different stages in the development of a protozoon. These bodies occur in the epithelial cells of the skin and tongue, between these cells, and free in the superficial lymph vessels and spaces of the corium (see Plate LXII.). For description they may be divided into two groups.

"The first group consists of a series of bodies varying in size from 2 to 7 μ. Structurally they are composed of a finely granular, closely meshed reticulum. Sometimes they contain small vacuoles. Their frequently irregular and elongated forms suggest fixation while in amœboid motion.

"The bodies of the second group are radiated in structure and measure 4–6 μ in diameter. They contain a central body from which radiate a comparatively large number of narrow segments. All stages occur between radiate bodies or rosettes just forming, and others where the segments are enlarging and leaving the central body to form the small granular forms already described.

"These bodies are brought out best by staining in eosin followed by alkaline methylene blue after fixation in Zenker's fluid. They stain a clear blue in fairly well-marked contrast to the purplish nuclei and the pale pink protoplasm of the cells. Other staining methods give no differentiation of the bodies.

"The evidence that these bodies represent different stages in the growth of a protozoon is based on morphological data only, and necessarily is far from conclusive.

* This communication and the accompanying photograph were not received until the main article had already been set up in type. —EDITOR.

EXPLANATION OF
PLATE LXII.

EXPLANATION OF PLATE LXII.

FIGS. 1 and 2 show numerous large and small scarlet-fever bodies in and between the epitheliai cells of the rete mucosum. In Fig. 1 is a large body in a lymph space of the corium just underneath the epidermis. Several of the bodies suggest fixation while in amœboid motion.

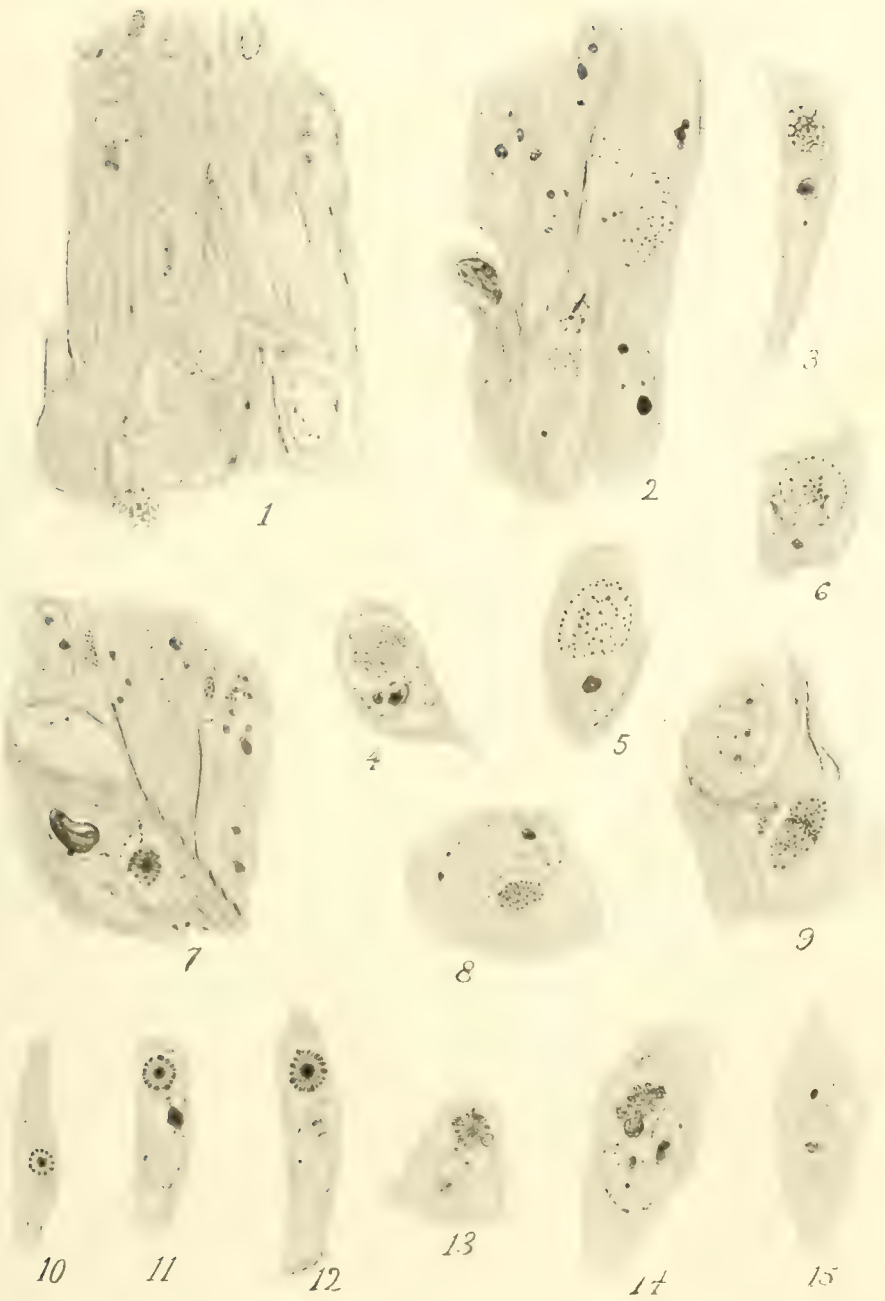
FIGS. 3, 5, and 6 are coarsely reticulated forms which may be degenerated forms of the scarlet-fever bodies, or stages in sporogony.

FIGS. 4, 8, and 9 probably represent stages preceding the radiate bodies. In Fig. 9 the bodies lie in a lymph space. It shows also four small forms which apparently have just freed themselves from a rosette.

FIGS. 7, 10, 11, 12, 13, 14, and 15 show different stages in the development of the radiate bodies.

FIG. 10 is the earliest stage; there is a distinct central body and a definite regular arrangement of granules at the periphery. Figs. 7, 11, and 12 show a little later stage of development; 11 and 12 are optical sections, while 7 is a surface view. Moreover, in Fig. 7 the body lies free in a lymph space in the corium. The segments begin to show a certain amount of lateral separation from each other.

Fig. 13 is a still later stage; the segments are increasing in size and are more or less free from each other, although most of them are still attached to the central body. In Fig. 14 the segments are all free and enlarging, although still grouped around the central body. In Fig. 15 three bodies are still grouped around the central body, which is free.



PROTOZOON LIKE BODIES FOUND IN FOUR CASES OF SCARLET FEVER

AFTER F. B. MALLORY

Journal of Medical Research, N.S. Vol. X, 1904

Their discovery may, however, prove to be the first step in clearing up the etiology of scarlet fever.

"Morphologically the bodies resemble fairly closely the different stages in the sexual development (schizogony) of the malarial organisms. Comparing them with the tertian malarial parasite under the same conditions of fixation and staining, they seem to be about one-third larger, and to have about twice as many segments in the rosettes.

"The accompanying illustrations (Plate LXII.) are a copy in black and white of the plate of colored drawings in the original paper."*

While these bodies must be studied in the living condition to demonstrate beyond question their protozoan nature, and while still further evidence must be adduced before their etiological relation to scarlet fever can be regarded as demonstrated, yet Dr. Mallory's work is of great importance and a strong presumption in favor of the view which he advocates. For his courtesy in furnishing these results in advance of the appearance of the article itself sincere thanks are due. *H. B. W.*

RADIUM.—Radium is a radioactive substance supposed to be a new element. Professors Curie and Demarcay have isolated in small quantity and tested what they consider to be pure radium, obtaining from their samples a characteristic spectrum, and have determined the atomic weight to be 225. On account of the rarity and great difficulty and cost of isolating radium it is used in the form of a bromide or chloride.

Discovery.—The discovery of radium is due to investigations upon radioactive substances. In 1896 M. Henri Becquerel, member of the Institute of France, reported the discovery that uranium gave off radiant energy having many of the properties exhibited by the radiations from x-ray tubes.

The radiations from uranium were given the name of Becquerel rays, from the distinguished scientist who discovered them. These rays have the property of discharging electrified bodies and of producing chemical changes in the silver salts ordinarily used in photography, in these respects being similar to the x-rays.

Uranium was first discovered in 1789 by the German chemist Klaproth, and named by him from the planet "Uranus." Uranium, though widely distributed, is never found in large amounts, and forms several minerals. The most common of these is uraninite, commonly known as pitchblende. It contains about eighty per cent. of uranium. The pitchblende which contains the largest amount of radioactive substances is the Bohemian pitchblende; but it is also found in Saxony, Cornwall (England), and in Colorado (United States).

Professor Curie and Mme. Curie, in investigating the Becquerel radiations from uranium found that some samples of pitchblende, from which the uranium had been extracted, gave forth radiations much more powerful than any they had found, having, in fact, four times the radioactivity of metallic uranium. They concluded that uranium being absent, the radiations were due to some unknown substance in the pitchblende, and following out this they discovered, in 1898, a substance to which they gave the name of "polonium." Polonium passes more rays through aluminum than uranium does, but these rays do not penetrate glass, are readily absorbed by minerals, and are cut off by thin paper. In the same year, following up the discovery of polonium, M. and Mme. Curie and M. Bemont isolated a second substance from pitchblende which possesses many of the chemical characteristics of uranium, but is much more powerful. To this they gave the name "radium."

Properties of Radium.—Radium is one of the most peculiar substances known to science, and produces phenomena which were hitherto unknown as existing in any chemical element or chemical combination: (*a*) It glows constantly with a visible light; (*b*) it gives off constantly a certain degree of heat; (*c*) it produces electrical effects similar to those produced by the x-rays; (*d*) it causes certain chemicals to fluoresce; (*e*) it reduces the silver salts ordinarily used in photography; (*f*) it transforms white into red phosphorus, and produces other transformations, such as changing the color of glass, porcelain, white paper, rock salt, etc.; (*g*) it has a distinct effect upon living tissue.

Nature of Radium Radiations.—The discovery of x-ray radiations and radium radiations has given rise to many ingenious theories, but experiments appear to show a distinct difference between radium rays and x-rays and the emanations from radium. Radium rays like x-rays pass through glass and substances opaque to ordinary light, while radium emanations are of peculiar character and appear to be more like a vapor. These emanations do not pass through glass, but settle upon all objects with which they come in contact, and like vapor of water may be condensed by extreme cold. The emanations from radium produce radioactivity in other substances, the result being, so far as is known, that all substances may be rendered radioactive through the influence of radium emanations. Substances so rendered radioactive present to a degree all the phenomena which radium itself presents, and when so charged retain the properties of radium for varying periods of time. The Curies have determined that substances thus rendered radioactive retain their induced radioactivity very much longer when guarded in a small enclosure through which the emanations cannot pass. In such cases the induced radioactivity diminishes one-half every four days, while in substances not so guarded it diminishes one-half every twenty-eight minutes.

Nature and Measurements of Radium Radiations.—There are three entirely distinct types of rays emanating from radium. These are known as the "α," "β," and "γ" rays. The α rays are the least penetrating, losing about one-half of their intensity if passed through aluminum 0.0005 cm. in thickness. The β rays are much more penetrating and much longer, and correspond in every particular to the characteristics of cathode rays. They are readily deflected by a magnet, discharge electrified bodies, etc.

The γ rays are the rays possessing the greatest penetrating power. These rays will produce radioactivity through the air at a distance of four feet or more, and are so much more penetrative than α rays that they require aluminum 8 cm. in thickness to reduce their intensity one-half.

The radioactivity of radium compounds is measured in terms of uranium, this element being taken as a standard. Professor Curie states that pure radium possesses one million times the radioactivity of uranium, but from the rarity of the substance and the difficulty of obtaining it in a pure form, the radium compounds which have so far been available for experiment have rarely been above a radioactivity of 7,000. The quantity of radium and radium compounds so far produced has been exceedingly small and the cost is very great. Professor Curie states that it would take five thousand tons of uranium residue to produce a kilogram of radium at a cost of about $2,000 per ton.

Heat-Producing Properties.—Radium has the remarkable property of maintaining its temperature at about 1.5° C. above its surroundings. Heat production like light production from radium appears to be made without any change in the radium and without any loss of weight. This remarkable force production as exhibited by constant heat production can be appreciated when it is understood that radium radiates enough heat to melt more than its own weight of ice every hour, and to continue, so far as is known, this force production for an indefinite period.

Light and Fluorescence.—When a tube containing radium is viewed in the dark it is seen to emit a distinctly visible light. The light emitted is of uniform quality and is produced indefinitely, and, so far as is known, without any change in the radium itself. When the rays from radium are directed upon the double cyanide of platinum and barium, tungstate of calcium, and certain

* Mallory: "Scarlet Fever. Protozoa-like Bodies Found in Four Cases." Journal of Medical Research, No. 4, vol. x., 1904.

other chemicals which fluoresce under the action of the *x*-ray, the radiations from radium cause these substances to glow with a visible light; the properties of the radiations from radium in this respect being like those from the *x*-rays. A sufficient quantity of radium has never been obtained to allow of the practical use of the fluorescence so obtained in the way in which the fluoroscope is used with *x*-rays, but it is possible that with a sufficient quantity of radium a fluorescence equal to that of the *x*-rays could be produced.

Photochemical Effects.—When the rays from radium are directed upon a sensitized photographic plate from which all ordinary light is excluded by having the plate enclosed in a light-tight envelope, the silver salts are reduced, and an effect similar to that produced by the *x*-rays is obtained.

This photo-chemical effect appears to be identical with that produced by the *x*-rays, except that either from the radiations from radium being less powerful in photochemical effect or from a sufficient quantity of the substance not being used, the rays have not as great penetrating power. Exposures of long duration produce outlines of the human hand with but faint indications of the bones.

Like the fluorescent effects of radium the photochemical effects have not as yet been made of practical value. Practical results may, however, be possible, provided radium can be obtained in sufficient quantities and its action can be properly controlled.

Vitochemical Effects.—The effect produced by the radiations from radium on living tissue are most remarkable. These effects, in certain ways, resemble the effects produced by *x*-rays, but appear also to have peculiar properties which, so far, have not been found to be produced by *x*-rays. Radium rays, like *x*-rays, are capable of producing "burns." The discovery of this effect of radium was made by Professor Becquerel, who, when journeying from Paris to London, carried in his waistcoat pocket a small tube of radium. About a fortnight later the skin under the pocket began to redden and fall away, and finally a deep and painful sore formed which was several weeks in healing. Like the burns produced by the *x*-ray these pathologic effects of radium radiations do not appear until several days after the part has been exposed. Many other important vitochemical effects are produced by the peculiar force thrown out from this remarkable substance. Becquerel found that if seeds were exposed for a long time to the emanations from radium their germinating power was destroyed.

M. Banysz, in experiments in the Pasteur Institute, found that the emanations from radium produced remarkable effects upon rabbits, guinea-pigs, and other small animals. These experiments show that radium has the remarkable power of so interfering with organic processes as to inhibit growth and even destroy life. A small amount of radium suspended over a cage containing mice will, after a few days, cause loss of hair and blindness, followed later by death. The same experimenter reports that exposure to the radiations from radium will cause arrest of development in certain lower organic forms. He exposed the larvæ of Ephestia kuehniella in a glass flask to the emanations from radium for a few hours. After a few weeks it was found that most of the larvæ were killed, but that a few had escaped the destructive action of the rays by crawling into distant corners of the flask where they were still living, but living as larvæ; whereas in a control flask similar larvæ had changed into moths.

M. Bohn has shown that radium may so modify various lower forms of life as to produce "monsters," and he has caused remarkable deviations from the original type in tadpoles exposed to radium emanations.

The vitochemical effect of radium seems to be particularly expended upon the skin and subcutaneous tissues and the nervous system. Thus, Danysz reports that the application of a tube containing a salt of radium to the skin produces an ulcer in from eight to twenty days. A few moments' application produces congestion of the human skin. When applied to the skin of a rabbit destruction of the epidermis follows, but when applied under the skin there is only a feeble reaction on the epidermis. Danysz found that when tubes containing radium were introduced into the intestines and serous cavities of guinea-pigs very little effect was produced, but its action was noted upon the nerve centres of all animals subjected to experiment. This action, however, was comparatively feeble in those whose osseous tissues protected the nerve centres. Application of tubes containing the salt to the cranium caused paresis, ataxia, and convulsions, followed later by death.

Professor Curie introduced a few milligrams beneath the skin of a mouse over the vertebral column, causing death of the mouse in three hours.

The rays of radium have a direct effect upon the optic nerve. This was shown by Giesel, who found that when radium salts were brought near the closed eyes a sensation of light was produced. This is attributed by Hammer to phosphorescence of the humors of the eye and also to effect upon the nerves of the retina. Prof. M. Javal proposes a diagnostic use of this phenomenon, and suggests that blindness with alteration of the retina can be distinguished from that due to glaucoma or corneal opacity, because patients with the latter condition see rays from radium as well as those of sound vision, while patients who have alteration of the retina have no sensation of light when a salt of radium is placed near the eyes.

Therapeutic Uses.—The vitochemical action of radium is so like that of the *x*-rays that its use for the cure of conditions for which the *x*-rays have been used was at once suggested. Experiments seem to show that the vitochemical action of the rays of radium are much more powerful than those of *x*-rays. There seems every probability, when radium can be produced in sufficient quantity and its action properly controlled, that it will be a valuable therapeutic agent. So far, its use has been mainly confined to the treatment of lupus, epithelioma, and superficial skin diseases. Favorable reports of results of its use in these diseases have been given by a number of clinicians. Danlos reports a case of lupus of the face, exposed to the action of a salt of radium which had a radioactivity of 19,000 for from twenty to thirty-six hours, with the result of the disappearance of the disease and with the formation of a smooth, white cicatrix. Other clinicians have reported equally favorable results and have called attention to the good effect as shown by the smooth, soft, and white resulting scar.

For therapeutic use the radium compounds have in some cases advantages over the *x*-ray. In superficial diseases of the skin and mucous membrane these radium compounds, being enclosed in small hermetically sealed glass receptacles, can readily be employed as therapeutic agents. All that is necessary is to place the receptacles containing the compound in close apposition to the parts, so insuring a local action. Furthermore, radium compounds being permanent these glass receptacles can be used for an indefinite time in any number of cases, and this apparently with more surety of definite results, so far as tissue reactions are concerned, than can be obtained from the radiations from *x*-ray tubes.

William Cline Borden.

SKIN AND ITS APPENDAGES: ANATOMY.—The skin, or integumentum commune, of the body acts as a covering and a protection for the deeper portions, besides being an organ of secretion, of excretion, of special sense—the sense of touch,—of common sensation, and the conservator of animal heat. Embryologically, it is developed from those two primitive layers of the blastoderm, the ectoderm and the mesoderm, which are formed by the cellular division of the impregnated ovule. The epidermis, or most external layer of the skin, is formed from the ectoderm, while a superficial portion of the mesoderm furnishes the remaining constituent parts—the corium, or cutis vera, and the subcutaneous or fatty tissue.

General Characteristics.—When fully formed the skin can be regarded as a completely closed sac, which

models itself so closely upon the portions of the body which lie immediately below it, that it allows their shape and configuration to be more or less accurately distinguished. This, naturally and to a great extent, will depend upon the amount of intervening fatty tissue. When the latter is present in excessive amount, symmetry and roundness of form dependent upon its presence in moderate quantity is naturally lost.

The skin does not stop abruptly at the natural openings of the body. It is continuous at these points with the mucous membrane which clothes the cavities. At the nares, on the labia majora and minora, and on the external surface of the anus, the transition of the skin over to the mucous surface is gradual, not abrupt. At the mouth, however, on the eyelids, and at the meatus urinarius, the transition is abrupt.

The integument is very variable in thickness. In general, it varies between 0.5 and 4 mm. ($\frac{1}{50}$ to $\frac{1}{6}$ in.), exclusive of the subcutaneous tissue. It is thinnest on the eyelids, and thickest on those portions which are subjected more especially to pressure, as on the palms of the hand and soles of the feet, or which serve as points of insertion for muscles, as on the upper lip, alæ nasi, etc.

Density and Elasticity.—It has been found that the skin possesses considerable solidity and very perfect elasticity. Sappey concluded from his experiments that a strip of skin 3 mm. long and 10 mm. broad was able to support a maximum weight of 12 kgm. (26½ lb.). The solidity was also in direct ratio to the thickness of the piece of skin used in the experiment. As mentioned, the elasticity is very perfect, but slight; a considerable amount of stretching may result from the application of a small weight, and complete rectification takes place after its removal. The skin is not of uniform texture, but consists of bundles of connective-tissue fibres arranged like a net, between which are spaces of various sizes which are rhombic in shape. In these spaces there is found a cementing substance, and it is due to it and the enormous network of elastic fibres that the former are able to regain their natural shape after having been stretched.

Cleavage.—The cleavage lines of the skin were demonstrated by Langer. He pierced the skin with small, round awls in multiple places, and, after removal of the instruments, observed that the wounds which were made were linear. He then made series of them in rows and close together, and from uniformity in the direction of the long axes of a more or less greater number of them, he was able to conclude that the skin possessed complete linear cleavage over the greater part of the surface of the body. Not on all of it, however, for in some places, as on the forehead, on many points on the scalp, etc., the wound made was a triangular one, and he found that these occurred where two spaces met together which possessed linear cleavage in opposite directions.

The explanation of the fact that the skin is, to a great extent, cleavable linearly, is to be found in the arrangement of the spaces between the bundles of fibres. These spaces are of various sizes and shapes, and in many places are so stretched longitudinally and so narrowed that the fibre bundles run almost parallel to each other. The course of the cleavage lines of the skin can be well understood by consulting the accompanying figure (Fig. 5195).

Tension.—Except upon the scalp, the palms of the hands, and the soles of the feet, the skin is, more or less, in a state of tension. When a portion is excised, it will be seen that it diminishes in size to such an extent that it will no longer cover the surface which has been laid bare. This cannot be ascribed entirely to the retraction of the borders of the wound, but is also due to the diminution in size of the excised piece, which is then no longer subjected to its former tension. Where the skin possesses linear cleavage, the tension is in the direction of these lines; but where this condition does not exist, it occurs uniformly in every direction in the plane of the surface. The tension likewise depends upon the movements of the joints and muscles, the amount of fat deposited in the subcutaneous tissue, and also upon morbid conditions, such as œdema, or upon the existence of pregnancy. In this latter condition the degree of tension may be so great that a permanent change may result in the direction in which the bundles of fibres run.

Color.—The color of the skin differs according to the individual, the race, and the age, and it also varies upon different portions of the body. It cannot be ascribed in certain races to climatic influences alone, since in the same zones people of different color are found, as in Africa, negroes, and in a corresponding portion of America, the much lighter colored Indians. The difference in color depends entirely upon the amount of pigment present in the rete Malpighii, where, under the form of granules, it is found especially in its lower layer or stratum basale. This is easily demonstrable in the skin of the negro two or three days after death, and before decomposition has set in. If the skin is, under such conditions, sharply rubbed, the epidermis is detached and rolls up under the finger, and the corium or true skin is seen to be of a dull white color. In the white race the color changes, within certain limits, in the various seasons of the year. When the skin is exposed to the heat and the sun in summer, there is an increase in pigment deposit and it appears darker, but this disappears and the whiter color returns in winter.

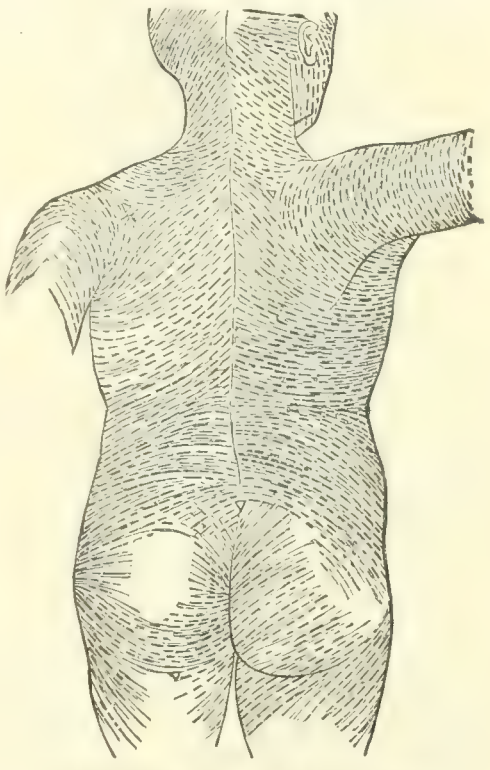


Fig. 5195. Cleavage Lines of the Skin. (Langer.)

Under certain physiological conditions, such as pregnancy, there is likewise an increase in the amount of pigment in particular portions of the skin—the areola around the nipple, the linea alba, etc.—and this may in some instances be to an exaggerated extent. A large portion of this increase often disappears after the birth of the child, but a considerable amount usually remains. In the male the scrotum and penis, and in the female the vulva, are of a darker color than the rest of the skin. The pink or red color seen on certain portions of the body, as the cheeks, or induced by certain temporary causes, as those which produce flushing, is due to the blood in the vessels of the cutis. These latter becoming filled with blood its color is conveyed to the eye through

the epidermic covering. When venous congestion is present the color is more or less of a bluish tinge. In old age the skin acquires a more or less yellow color, due to the atrophic changes that take place in it, and also to the lesser amount of blood supplied to it.

The Folds and the Furrows of the Skin.—Many furrows are seen on the skin. Some are long and deep, others are short and shallow. The former are present to a great extent from birth, and are seen running in a transverse direction across the extensor and flexor surfaces of joints.

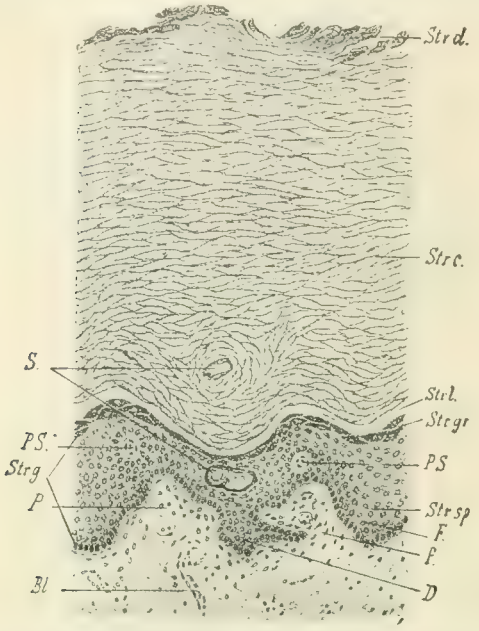


FIG. 5196.—Section of the Skin (epidermis and the papillary portion of the corium) on the Sole of an Adult Foot. Specimen hardened in a solution of picric acid and bichloride of mercury, and stained with hæmatoxylin and eosin. Magnified 90 diameters. (After Rabl.) *Str d.*, Stratum disjunctum; *Str c.*, stratum corneum; *Str l.*, stratum lucidum; *Str gr.*, stratum granulosum; *Str g.*, stratum germinativum; *Str sp*, stratum spinosum; *F*, fold of epithelium; *D*, glandular ridges; *S*, outlet channel of a sweat gland; *P*, papillæ; *Bl*, blood-vessel.

The latter are represented by the wrinkles on the face which develop with age. These latter are due partly to the diminished elasticity and turgescence of the skin, but they are induced more often by muscular contraction and stretching of the cutis.

The furrows around the joints are produced by the movements of flexion and extension. They are not able to overcome directly the tension of the bundles of fibres, which in this situation run transversely or obliquely across the joints; in consequence the fibre bundles are not stretched by the ordinary movements, but the rhomboidal spaces between them are. On one side of the joint their tension is in the direction of their breadth, while on the opposite side the fibre bundles are brought closer together. In this way the constant furrows around the joints are caused. Those which are due to muscular action, as the wrinkles on the forehead, etc., are produced in the same manner, the constant repetition of the movements finally effecting a permanent change in the arrangement of the fibre bundles and of the spaces between them.

The folds seen in very emaciated persons are likewise caused by the diminution in the size of the rhomboidal spaces. This is brought about by the loss of fat and the consequent change in the arrangement of the fibrous structure of the skin. Coarser furrows are also seen on the palms of the hands and on the soles of the feet, and in these places the skin is not movable. These furrows are always permanent, being caused by the firm union of the skin to the tissues below by means of short bundles of connective-tissue fibres. Dimples, where they occur, are due to the same cause; that is, the skin is at that point attached to the underlying tissues and does not move together with the rest of the skin of which it forms a portion.

THE STRUCTURE OF THE SKIN.—The integument of the body is composed of several layers. The most external of these consists of epithelium and is termed the epidermis. It clothes the outer surface of the corium, or cutis propria, the line of division between the two being very sharply defined and great morphological difference exists between the elements composing each. The corium is a closely knit tissue, consisting of connective tissue, elastic fibres, and unstriped muscle. It contains the glands of the skin and the hair, and is rich in blood-vessels and in nerves. It is not sharply limited on its under surface, but goes over here gradually into the subcutaneous or fatty layer of the skin. This layer, the panniculus adiposus, is in reality the deeper portion of the cutis, and consists of connective-tissue fibres loosely put together, which contain in their cells and in the spaces between them a more or less large amount of fat.

The epidermis and the corium are the most important portions of the skin, and vary in many particulars on different portions of the body. The various appendages of the skin—the hair, the nails, and the glands—are derived from or are attached to them.

EPIDERMIS.—*Embryology.*—The epidermis, the most external layer of the skin, is formed from the ectoderm, and in the first month of life and the beginning of the second consists of only a single, or in its thicker portions of two or three rows of polygonal cells. Below these is a layer of very small cells, which represent the origin of the stratum mucosum or rete Malpighii. This increases, in the course of development, to several rows of cells, the layer becoming more and more distinct and thicker. In the mean time the outermost cells have also become flatter, and represent the primitive horny layer, which, however, remains during fœtal life of a low grade. It is subjected to constant desquamation, and the scales from its surface are mixed with the secretions from the skin to form the vernix caseosa. As early as the eighth month (Unna), granular cells begin to appear between the horny and mucous layers, and the cornification of the epidermis cells becomes more marked. Nevertheless, and before this, the horny layer has become strong enough to oppose sufficient force to the epithelial growth and to the proliferation of its cells, so that the increase in thickness of the rete Malpighii can no longer take place in the direction of the external surface, but is compelled to proceed downward toward the cutis propria. It penetrates, in its further development, into the spaces between the rudimentary papillæ, springing from the surface of the cutis, and thus forms the interpapillary prolongations of the epidermis. It is by virtue of these ingrowths of the epidermis that, when fully formed, it lies upon the derma as an accurately fitting coat, which follows closely the outlines and inequalities of the true skin.

Thickness of the Epidermis.—The thickness of the epidermis, as a whole, varies from birth to old age, on different parts of the body, and is also influenced by external causes, as pressure, rubbing, etc. At birth it is from 0.15 mm. to 0.25 mm. in thickness, but in adult life from 0.75 mm. to 1.66 mm. The differences are due, for the most part, to the thickness of the horny layer, which in some situations, as on the palms and soles, or on any surface subjected to constant pressure, may attain a very considerable increase in thickness.

Layers of the Epidermis.—The epidermis is divided into two major layers, due to the different consistence of the cells constituting each. The most external and superficial one, consisting of horny cells, is firm and resistant, and termed the stratum corneum, while the one immediately below it, lying in contact with the derma, is called the stratum mucosum, or rete Malpighii. The latter consists of soft epithelial cells and is sharply defined from the stratum corneum. Both of these major layers are still further subdivided according to the ap-

pearance of its cells, or to the reaction of their various portions to certain coloring substances.

Rete Malpighii.—The most deeply situated cells of the stratum mucosum, those which are in immediate contact with the derma, are cylindrical in shape and form the basic layer or stratum basale of the rete. Its importance can be estimated from the fact that it represents the productive part of the stratum mucosum. In normal skin they are the only cells which show the karyokinetic cell figures and indirect division of the nucleus occurring in epithelial growths. Their long axes are directed perpendicularly to the corium, and if the layer is carefully examined, small basic cells, resulting from the cell division, are seen pushing their way in between the older ones.

The cylindrical cells send out into the corium more or less long prolongations, but the spines, which characterize the entire rete, are seen clearly only upon their upper contours. It is in these cells, especially, that a more or less large amount of pigment granules are deposited, which give the various shades of color to the skin of different individuals and races.

Above the basic layer, cells of various shapes and sizes are found. Over the papillæ, and in the interpapillary portions of the rete, round and cuboid and polygonal cells are seen. In the interpapillary prolongations, however, round cells predominate. As the external surface is approached the cells become larger, and have their long axes more parallel to the surface of the skin. The cells themselves have a body consisting of finely granulated protoplasm, which contains a clearly defined nucleus, in which are several nucleoli. According to the position of the cells in the rete, the shape of the nucleus varies. In the uppermost portions it is oval, in the middle, round, and in the cylindrical layer, rod-like, thus agreeing more or less accurately with the shape of the cell. The varying form of all of these cells is due in general to the degree of mechanical pressure to which they are subjected by the individual growth of each, and by other causes, such as atmospheric pressure. The cells composing this portion of the rete Malpighii do not lie in close contact with each other, but are held in apposition by protoplasmic prolongations from their surfaces, which are continuous with the protoplasm of the cell body. They have been termed spines. It is due to this characteristic that the entire layer has been named the stratum spinosum.

The spines, which characterize these epithelial cells, were first observed by Schrön, and the function of binding the cells together has been attributed to them. The manner in which this occurs has, however, always been a subject of controversy. Max Schultze was of the opinion that they were arranged as in a pinion and ratchet; Bizzozero, that their ends were united together; and Ranvier, that their ends were fused together, forming a peculiar elastic organ which allowed considerable movement. These spines can be studied best in rapidly proliferating growths of the rete, as in condylomata acuminata; but in the normal skin it is very difficult to form any opinion in regard to their natural arrangement. Whether the spines are active or passive in their nature is likewise a disputed point. Still, as Unna has pointed out, they are in all probability the result of active protoplasmic movement, since they are purely prolongations of the cell body and consist of the same protoplasm.

Intercellular Spaces.—The arrangement of the spines springing from the surface of the cells of the rete is such that small spaces are left between them. These, the intercellular spaces of the stratum mucosum, are of great importance, inasmuch as they serve as channels for the passage of the nutrient fluids from the corium to the epithelium. The communication existing between the blood and lymph vessels and spaces and these intercellular spaces was clearly demonstrated by Nalepa, who succeeded in injecting them from the subepithelial blood-vessels. The wandering cells coming from the vessels of the cutis and seen in the rete are also enabled to wander along by means of these spaces, and they are the source of the pigment sometimes seen in these situations.

Stratum Granulosum.—Situated above the stratum spinosum, but yet in close contact with it, is a layer of cells characterized by the possession of certain peculiarities. This layer consists of one or two rows of cells, seldom of more, upon whose surfaces shortened spines may still be seen, and they also contain granules of various sizes and shapes. It is owing to the presence of these that it has received the name of stratum granulosum. These granules react toward certain coloring substances in a marked manner, and stain very deeply. Unna, who has studied this layer very carefully, states that it makes its appearance in the epidermis toward the end of fœtal life, but that it can be seen much earlier in the inner root sheath of the embryonic hair.

The stratum granulosum is present over the entire skin, except on the vermilion border of the lips and in the nail bed. The granules appear white by direct light, and for this reason Unna asserts that they are the cause of the white color of the Caucasian race. Such an explanation is, however, scarcely a reasonable one, owing to the fact that this same stratum granulosum is present in the skin of the negro as well as in that of the other dark races; and besides, when it is found pathologically or even under natural conditions greatly increased in depth, it does not seem to cause the color of the portions where it is situated to be whiter than the remainder of the skin. The stratum granulosum is very marked in condylomata acuminata and on the palmar surface of the hands, and yet the former are far from being white in color, and the latter are not especially so.

The granules which are present in these cells have been the subject of so much discussion that they are worthy of extended consideration. They were observed long ago by Kölliker in the medulla of the hair, and by Aufhammer in the epidermis. Langerhans, however, was the first to describe them carefully, while Unna pointed out that they stood in constant relationship to the process of cornification, and he claimed that they represented the intermediate steps which occurred in this process, transforming the soft epithelial cells into horny tissue. Ranvier regarded them as drops of a fluid substance, which existed in a free state in the lowest layers of the stratum corneum, and to which he had given the name of eleïdin. Waldeyer, however, has furnished the most satisfactory and correct information in regard to them. He proved that they could not be drops of fluid, because they swelled up on the addition of alkalies and also changed their shape on pressure, but not in the manner that fluids do. They were likewise insoluble in ether, alcohol, or water, and possessed a very great affinity for the nuclei-staining dyes, as hæmatoxylon, picrocarmine, etc. The supposition that they were fatty in character was also excluded by their want of reaction to osmic acid. Waldeyer found, on the other hand, that they agreed chemically very closely with the hyalin of Recklinghausen, a product of degeneration, and for this reason he suggested the name of keratohyalin for the substance.

Keratohyalin, according to Unna, is found to a small extent around the nucleus of the cells in the middle portion of the stratum spinosum, but it exists to a considerable extent only in the stratum granulosum. The granules here are small, and though the cells are filled with them, yet a small peripheral zone always remains free from encroachment. The cells in this layer have atrophied nuclei, which, however, still stain well, and the intercellular spaces are narrowed to such an extent as to be almost entirely absent.

The significance of keratohyalin and its relation to the process of cornification have received much attention. The general opinion at present is in favor of regarding these granules, not as the cause of the cornification of the rete cells, but as a phenomenon accompanying that process, and as one which is produced by the act of cornification taking place in the periphery of the cells.

Stratum Corneum.—The layer of the epidermis lying above the stratum granulosum is the stratum corneum.

It is the one which is most external and is in contact with the air. It varies greatly in thickness on different portions of the body, being, however, usually most marked on the palms of the hands and on the soles of the feet, and also being always much increased on any portion of the skin which is subjected to constant pressure. On these surfaces especially, but not exclusively—that is, on the palms and the soles—it is noticeable that its lowest portion, that which is immediately next to the stratum granulosum, possesses great transparency. This stratum is narrow, sharply defined, and is known as the *stratum lucidum* of Oehl, but its existence has never been satisfactorily explained. The cells forming the stratum corneum are clear and transparent, showing neither granules nor nuclei. Unna claims to have found traces of the spines seen on the cells of the stratum spinosum even here, and asserts that the coherence of the cells forming the horny layer is due to their persistence.

By means of artificial digestion with pepsin and trypsin, it has also been found that the entire cell does not become cornified, but only the peripheral portions. After employment of this method it is clearly seen that it is the contents of the cells which are destroyed, while the peripheral portions remain and have the appearance of horny shells.

The reaction of the epidermis to certain staining materials allows furthermore a recognition of several layers constituting it, and shows successive changes not only in the cell substance, but also in the intercellular spaces. We owe to Unna the following table, showing the reaction of the several layers of the epidermis to various dyes:

Layers of the epidermis.		Consistence.	Osmic acid.		Picrocarmine.	Hæmatoxylon (glacial acetic acid).	Iod violet only slightly decolorized).	Salicylic acid—chloride of iron (H. Hebra).
			Without removal of fatty matter.	After removal of fatty matter.				
A. Stratum corneum	1. Superficial	Firm	Black	Clear	Yellow	Bluish-white	Blue	Brown.
	2. Middle	Looser texture	Clear	Dark brown.	Red	Violet		Clear.
	3. Suprabasic	Firm	Black	Clear	Dark red	Bluish-white	Clear	Light brown.
	4a. Basic, stratum lucidum of Oehl.	Very firm			Yellow		Blue	Not constant.
	4b.		Clear	Dark brown.				
B. Stratum granulosum		Soft	Protoplasm		Granules colored dark red	Granules colored violet.		Brown.
C. Stratum spinosum	Rete Malpighii, stratum of Fleming.		Coloring (green).		Nuclei colored dark red.	Nuclei colored blue.	Nuclei colored blue.	Light brown.

The several layers which have just been described as entering into the formation of the epidermis should be carefully considered in the study of the anatomy of the skin. It is from the epidermis that the appendages of the skin, the hair, the nails, and the glands, originate and derive their most important parts. We shall refer to this again when describing these various constituent portions of the skin.

The Corium, Derma, or Cutis Propria.—*Embryology.*—The corium, or true skin, is that portion which lies between the epidermis and the subcutaneous or fatty layer. It is derived from a superficial portion of the mesoderm, consisting at first of only round cells. In the second month of fœtal life, however, spindle-shaped cells begin to appear, but only very little intercellular substance is present. Very shortly after this, it is noticed that the cells in the upper portion of this primitive corium become more closely aggregated together than in the lower portion, and at the same time the formation of fibrillated tissue begins in this latter. The fibres increase greatly in number, and by the fourth month the presence of fat is detected. It is in this way that the subcutaneous or fatty layer is developed, and it is to be considered, in reality, a part of the derma, since it has the same embryological source, and not a separate and distinct layer of the skin. The transformations which take place among the closely aggregated cells in the upper portion are shown by the penetration of fibres between them and by the deposition of collagenous material. The individual cells are thereby more and more widely separated from each other, and the corium attains a considerable degree of thickness. Gradually blood-vessels and nerves pass into it, and upon its superficial surface the papillæ begin to form. These latter appear about the sixth month of fœtal life as small eminences upon the surface of the cutis. They are formed by the growth of the epidermis, which pushes before it the weaker and more yielding portions of the cutis. They are first seen on the palms of the hands and the soles of the feet, but are quite general toward the end of fœtal life. The development of the papillæ is not fully completed until after birth.

Divisions of the Cutis.—The major part of the cutis consists of fibrous connective tissue, which is poor in cells and which is arranged in the form of bundles. The texture of the cutis is closely knit in that portion which is next to the epidermis, but is much looser in the parts below this. In this situation, the fibre bundles crossing each other form the rhombic spaces, which have been mentioned as the cause of the linear cleavage of the skin. On account of the difference in the texture of the cutis, it has been divided into two layers: the one in immediate contact with the epidermis being termed the pars papillaris, that below it, the pars reticularis.

Pars Reticularis.—The pars reticularis of the corium is composed of bundles of fibres of various sizes and lengths. They are continuous with the connective tissue of the inner portions of the body—the fasciæ, etc.—and pass upward perpendicularly, or slightly inclined to the surface of the skin, until they arrive at the cutis. Here they run obliquely, crossing each other at various angles, and serve as boundaries for spaces which are formed by their intersection. These spaces are, in general, rhomboidal in shape, but oftentimes polygonal, their regularity depending upon the length and uniformity of course of the fibre bundles forming them. The length of the fibre bundles and the absence of their firm adhesion to the underlying tissues are very important factors. It is owing to such an arrangement that the skin is freely movable over the greater portion of the body. On the scalp, the palms of the hands, and the soles of the feet, where these bundles of fibres are short and intimately united to the underlying fascia, the skin is only very slightly movable. These places of intimate union, however, serve as fixed points from which the skin is stretched over the body. The movability of the skin is also limited on the circumscribed portions, where it is in immediate contact with bone, cartilage, or tendons, as over the tibia, etc.

The bundles so frequently mentioned are composed of fibres, which correspond in structure to those of fibrous connective tissue. Under normal conditions they are in

a state of tension, and are for the most part straight, but under the microscope they are found presenting a wavy appearance. Chemical examination has shown that they consist to a great extent of collagenous material. The fibres themselves are bound together in bundles by an albuminous semifluid cementing substance, which Rollet has found to be similar to mucin. According to Fleming, this cementing substance not only exists between the fibres, but also surrounds the bundles, and Tomsa claims that it binds together all the constituents of the cutis.

The fibres possess cells, but they are numerous only in the vicinity of the large blood-vessels. These cells are the usual connective-tissue cells; they are large and contain nuclei and nucleoli. They lie upon the bundles in the same manner as endothelial cells do in the situations where these are found, and for this reason have at times been regarded as forming an endothelial lining for the rhombic spaces between the bundles. It has, however, been demonstrated that they differ from the cells of endothelium in that their edges do not lie in contact with each other, and they do not form a continuous covering for the bundles (Ranvier).

Elastic Tissue.—According to the latest investigations made in regard to the elastic fibres of the skin—a most thorough study of which has been made by Unna—they are exceedingly abundant in the reticular portion of the cutis. By the use of special methods of staining and of preparation, Unna found that, under the form of broad bundles, elastic fibres spring from the fascia below the skin, and, passing up between the fat masses, penetrate into the cutis. In their course they divide continually in a more or less forked manner. These bundles may be traced upward to just below the epidermis. The muscles of the cutis also serve as points of origin for bundles of elastic fibres, and Unna claims that they can be seen attached to the muscles at their points of origin and insertion, having a tendon-like appearance.

FIG. 5197. Two Papillæ of the Skin of the End of the Toe. The elastic fibres which they contain have been rendered specially distinct by the use of Weigert's method of staining. This method, while causing the elastic fibres to assume a deep black color, makes all the surrounding tissues appear pale blue. The specimen was hardened in alcohol. *P.* Papilla; *F.* fold of the epithelial layer; *D.* glandular epithelial ridge; *Str.M.*, stratum Malpighii; *Str.c.*, stratum corneum; *S.E.*, subepithelial network of elastic fibres, which are especially abundant around the epithelial fold (*F.*, whereas on the sides of the glandular ridge the network is looser, *i.e.*, it contains decidedly fewer elastic fibres; *E.W.*, basal epithelial cells which are distinguished from the others by their darker coloring.

Another relatively fixed point of the elastic basework of the cutis is seen in an extensive network of fibres, which follows with the greatest regularity the outline of the epidermis, where this latter is in contact with the corium. This network, which Unna terms the subepithelial elastic net, is situated just below the surface of the cutis, being separated from the epidermis by a narrow homogeneous strip of the derma, in which there are very few blood-vessels. From this network fine fibres are given off, which proceed upward perpendicularly and are lost sight of here and there between two of the basic epithelial cells of the epidermis.

There is, also, in the papillary portion of the skin, an extensive network of elastic fibres. It is formed by the repeated division of fibres which originate from the subepithelial network. All of these elastic fibres do not exist independently of the rest of the cutis, but are more or less closely connected with the fibre bundles of connective tissue which have already been treated of.

The relationship of these elastic networks to the appendages of the skin, such as the hairs and glands, has not yet been thoroughly studied. Still Unna claims that there is some special connection between them and the sweat ducts and glands. The elastic fibres are found to be entirely absent around the coils, but quite abundant about the ducts, along which they run in a parallel direction. He consequently is of the opinion that the contraction of the elastic network of the skin, acting with the fibre bundles with which it is in close union, produces a pressure on the ducts, and shortens them by diminishing the thickness of the skin. In this way the passage of the secretion of the glands through the ducts to the outer surface is favored.

Unstriped Muscle.—With the exception of the palms of the hands and the soles of the feet, the skin of the entire body contains a more or less large number of unstriped muscular fibres and bundles. They are found to attain their highest development in the skin of the scrotum, in the penis, and in the nipple and its areola. The vermicular movements of the scrotum are due to these involuntary muscles, as is also the erection of the nipple. They are situated in the cutis propria, and lie perpendicular to the plane of cleavage of the skin. On the penis they are arranged in a circular manner, and they follow a similar course in the nipple and in its areola.

Besides these, there are other muscles in the cutis which, owing to the connection existing between them and the hairs, are termed the arrectores pili. They are formed by the union of several small muscular bundles, which, originating in the pars papillaris, run an oblique course through the reticular portion of the cutis, and are attached to the hair follicle. The point of their attachment is not uniform—sometimes to the middle portion of the hair sheath, sometimes low down in the lower third. It will usually be observed that in their course to their point of attachment, they curve around the sebaceous gland attached to the hair follicle and are in quite intimate connection with it. According to Tomsa, the fixed point of the arrector muscles is the hair follicle, while the point of movement is the pars papillaris of the cutis.

The arrangement of the involuntary muscular fibres in many places in the derma, as in the cutis of the forehead, cheeks, back, is in the form of a network. This net originates in the pars papillaris and is distributed throughout the upper two-thirds of the pars reticularis. By the action of these muscles the skin is kept more or less in a condition of tension. According to the direction in which they exert their action, the muscles have been divided into horizontal and oblique tensors. The elastic bundles and fibres connected with the muscles play here an important part, inasmuch as Tomsa has shown that they stand in the same relationship to them as do the tendons to the voluntary muscles, and serve as fixed points from which the contraction of the cutis tensors takes place. The action of these muscles also regulates to a great extent the circulation of the lymph in the cutis, while the contraction of the arrectores elevates the hair, compresses the sebaceous glands, and facilitates the propulsion of their secretion into the hair follicle.

The Pars Papillaris Cutis.—The papillary portion of the true skin is constituted by a series of small eminences or papillæ, which spring from its upper or free surface. It is in direct contact with the epidermis, which, as has already been described, sends down prolongations of epithelial cells between the papillæ.

The papillæ of the skin are found most fully developed on the palms of the hands and on the soles of the feet. They are arranged here in long double rows, which form the curvilinear ridges seen in these situations. Between these rows there is a narrow path in which are the external orifices of the sweat ducts. On other portions of the body the papillæ are arranged more or less in groups or in short rows, and the surface of the cutis seems to be divided into rhomboidal spaces of various sizes by the deeper penetration of the interpapillary prolongations of the epidermis. The long diameters of these spaces agree with the line of cleavage of the portion of the skin where they are situated, and their shape is dependent upon the arrangement of the connective-tissue bundles in the reticular portion of the cutis.

The papillæ are more or less conical in shape, sometimes single, or again cleft into two or more points, forming a compound papilla. They differ greatly in shape, size, and distribution on the various portions of the body, and also vary according to the age of the person (Unna), becoming in old age almost flat. They are very numerous on the penis, the nipple, the labia minora, and the clitoris, appearing in these places as low hills. The largest papillæ are found in the cutis of the nipple and of the corona glandis. Those distributed generally over the surface of the body are very small, about 0.05 mm. in height. On the ends of the fingers, under the free borders of the nail, they attain a size of 0.5 mm.; but their height varies in general between 0.05 mm. and 0.2 mm.

The papillary portion of the cutis consists of a closely woven network of fibres, which are derived directly from those forming the pars reticularis. The papillæ are very rich in elastic fibres, and contain blood-vessels, lymphatics, nerves, and, in certain situations, tactile corpuscles. The manner in which the papillary body and the epidermis are joined together must be studied on specimens which have been macerated, and from which the epidermis has been removed *in toto*. When this has been done, it is seen that the entire surface of a papilla has a finely ribbed aspect. On sections made horizontally through them, they look as though their contour was toothed. The ribs have a slightly wavy course and are at times arranged in a concentric manner, having much the same appearance as may be observed on the palmar surfaces of the ends of the fingers. These ribs on the papillæ have been found to correspond to minute furrows on the cells forming the basic or cylindrical epithelial layer of the epidermis and to fit into them, each cell requiring usually three or four ribs. From the fibrillated appearance it might be thought that these ribs were connective-tissue fibres, but such has been found not to be the case. They consist in reality of a transparent homogeneous substance, which covers thinly the surface of the papillæ. The proof that it is a distinct membrane has never been satisfactorily made, and it seems better to accept Unna's view, that it stands in intimate connection with the cementing substance of the cutis in general, since it has been found that, when the cutis is subjected to the action of trypsin, this homogeneous substance covering the papillæ disappears in the same way as the cementing substance in other portions of the derma.

The Subcutaneous Connective Tissue or Fatty Layer.—It was mentioned, in speaking of the embryological origin of the skin as a whole, that the subcutaneous or fatty tissue was derived from the mesoderm. It is that portion which attains its full development the earliest of all the layers of the skin, and in which the deposition of fat between the fibres constituting it takes place very early in fœtal life. The subcutaneous connective tissue, or panniculus adiposus, though in reality the lower portion of the corium, is regarded as forming the third layer of the skin, and it is characterized by the presence of a greater or less amount of fat included within its meshes.

It is composed of bundles of connective-tissue fibres, a network of elastic fibres, and of fat, and is very rich in large cells. These have long poles and are situated either in or between the fibre bundles, occurring in the form of spindle-shaped cells. According to Flemming, the masses of fat can be divided into three classes, each of which is characterized by its blood supply; the fat clusters with their own blood-vessels; the strands of fat which lie around the large vessels and receive only a meagre supply of blood from capillaries; and the fat islands which have no blood supply of their own. We have to thank the same investigator for our knowledge of the histology of fatty tissue. He found that the fat cells were derived from ordinary branching connective-tissue cells. They took up fat in small drops, and in proportion as the fat increased in quantity the protoplasm of the cells also increased, and they became round in shape. The protoplasm containing the nucleus is forced to the periphery by the accumulation of fat, and appears as a membrane; but these fat cells have no true enclosing membranes, except when they are old, and when the protoplasm has become thickened into a membrane-like covering. The contents of the cells do not consist of pure fat, but of a mixture of fat and of some product from the protoplasm. At the time of birth the panniculus adiposus is very greatly and uniformly developed over the entire body. As the child grows, however, it diminishes in quantity and remains of considerable extent only on certain portions. Its function is protection to the underlying tissues, and it serves to give roundness to the outline of the body. Those portions of the body which are firmly bound down to the fascia by short bundles of fibres, as the scalp, the skin of the palms and of the soles, etc., possess only a small fatty layer. Where great mobility is necessary, as in the eyelids, or where there is a great amount of muscular tissue, as in the scrotum, the panniculus adiposus is also absent. Over the joints, where the skin lies in close contact with the bones, and by their movements is continually subjected to pressure and tension, bursæ develop in the subcutaneous tissue after birth. In this layer the large arterial and nerve trunks going to the cutis are found, and also the veins and lymphatics which come from the derma and unite to form large efferent branches. In certain localities the Pacinian bodies are also present.

The Glands of the Skin.

There are two sets of glands which are found in the skin, the sweat glands and the sebaceous glands. They differ from each other to a most marked degree, and if considered from the standpoint of their relative importance the former claim priority and more extended study. We shall, therefore, begin with the sweat glands.

The Sweat Glands.—*Embryology.*—The primary evidences of the development of these glands of the skin

are seen in the fifth month of fœtal life. They appear first on the palms and on the soles, under the form of rows of epithelial prolongations from the inferior border of the epidermis into the cutis. At this stage they are solid, club-shaped, and surrounded by a homogeneous membrane. Their further development consists in the elongation of these epithelial ingrowths downward, and in the formation, by the seventh month, of a cavity along its axis, which is later further extended through the epidermis to the external surface. In the mean time, the gland tube at the end in the cutis has become coiled up; forming a ball, and the excretory duct in its course through the skin is twisted upon itself. The development of these glands is very rapid, and by the end of fœtal life they have already attained their full development. In certain situations, however, they enlarge even after birth, and in their structure differ somewhat from the ordinary and smaller ones distributed generally over the body. These larger glands are found in the axillæ, the inguinal regions, around the anus, the nipple, and in the auditory canal (ceruminous glands).

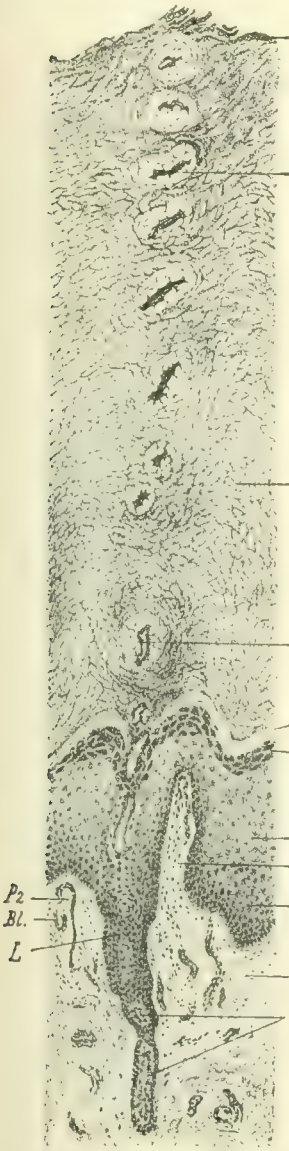


FIG. 5198.—Section of the Skin (epidermis and papillary layer of the corium) of the Sole of the Foot. Specimen hardened in Mueller's fluid; staining with hæmatoxylin and eosin. Magnified 60 diameters. (After Mracek.) *S*, Orifice and deeper tubular portion of a sweat gland; *Str.d.*, stratum disjunctum; *Str.c.*, stratum corneum; *Str.l.*, stratum lucidum; *Str.gr.*, stratum granulosum; *Str.M.*, stratum Malpighii; P_1, P_2, papillæ; *F*, fold of the epidermis; *L*, glandular portion of the epidermis; *Str.p.*, stratum papillare; *Bl.*, capillary loop in the papilla.

The sweat glands are present everywhere in the integument of the body, with the exception of the glans penis, the under surface of the prepuce, and the vermilion border of the lip. They are small bodies, consisting of a convoluted tube and an efferent duct which leads to the external surface, and they are situated in the corium or even in the subcutaneous connective tissue. They vary greatly in size. The coils of the large ones situated in the axilla are from 1 mm. to 2 mm. in diameter; the smaller ones on the general surface are from 0.2 mm. to 0.3 mm. They are most numerous on the palms of the hands, Krause estimating that there were twenty-eight hundred orifices in a square inch on those surfaces.

The sweat glands, as a whole, are composed of two distinct portions, a secretory and an excretory. The

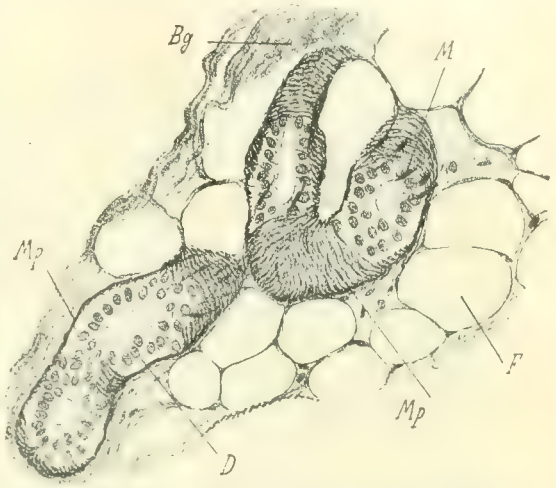


FIG. 5199.—Two Separate Portions of the Secreting Part of the Coil of a Sweat Gland, from the Skin of the Abdomen. Magnified 250 diameters. (After Mracek.) *D*, Gland cells; M_p, membrana propria, seen at one point in cross section, at the other as if spread out upon a flat surface; *M*, muscular fibres; *F*, flat cells; *Bg*, connective tissue. The specimen was hardened in alcohol and stained rapidly with orcein.

former is represented by the coils, the latter by the duct which leads to the external surface of the skin. The histological anatomy of the smaller glands differs somewhat from that of the larger ones, and will be considered first.

Histological Anatomy.—The coils, or secretory portions of the sweat glands, consist of a single layer of columnar epithelium, arranged around a rather irregularly shaped lumen. The cells are cloudy throughout, with the exception of a narrow portion along their free margin, which is clear. They are bounded externally by a layer of involuntary muscular fibres, which run spirally around the mass of cells, and which are so arranged that small spaces are left between them. The secreting cells send out processes into those spaces, and these form a union with the limiting membrane or membrana propria of the glands, which is composed of connective tissue. The excretory portion of the gland, or duct, consists of a connective-tissue coat, a structureless membrane, and bounding its lumen are two rows of epithelial cells, the free margins of which are covered by a cuticula. There are no muscle fibres in the coats of the sweat ducts. These latter begin in the inner portion of the coils, and rise to the surface in an oblique direction having a more or less spiral course, and they always reach the epidermis at an interpapillary prolon-

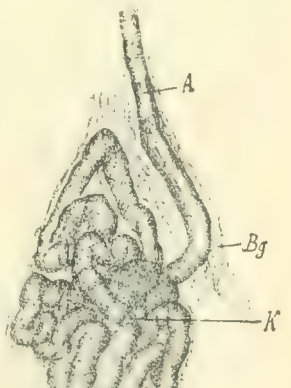


FIG. 5200.—Terminal Coil of a Sweat Gland, from the Skin of the Back of the Foot. Obtained by Professor Schaffer as a separate and complete specimen by maceration in diluted nitric acid. Magnified 80 diameters. (After Mracek.) *K*, Terminal coil; *Bg*, enveloping connective tissue; *A*, outlet of the gland.

gation. The duct here loses its membrana externa, which goes over into the tissue of the papilla, and also its cuticula, so that the lumen is bounded for a short distance in the stratum spinosum by the spiny cells alone. The cells which limit the lumen in its course through the epidermis, show granules of keratohyalin very early, and considerably below the level of the stratum granulosum; and it can further be seen that all the layers of the epidermis became interested and aid in forming the boundaries of this spiral canal in its course to the external surface. The views which are held by Unna, in regard to this portion of the duct, have so much in their favor as to claim general recognition. He does not consider that the spiral portion in the epidermis belongs entirely and alone to the duct of the sweat gland, of which it seems to be a continuation, but thinks that it is a canal which is also in connection with the system which conveys the juices throughout the epidermis. According to him, the sweat duct ends in the basic layer of the stratum spinosum, and he would, consequently, separate the two portions very sharply. He very rightly points out, in support of this, that we have no reason for concluding that the fluid which passes through it comes entirely from the same source, inasmuch as there are no grounds for asserting that the sweat is derived from the coils alone. All that we do know is, that it appears upon the external surface at the openings of these canals, but more than that has not been proved.

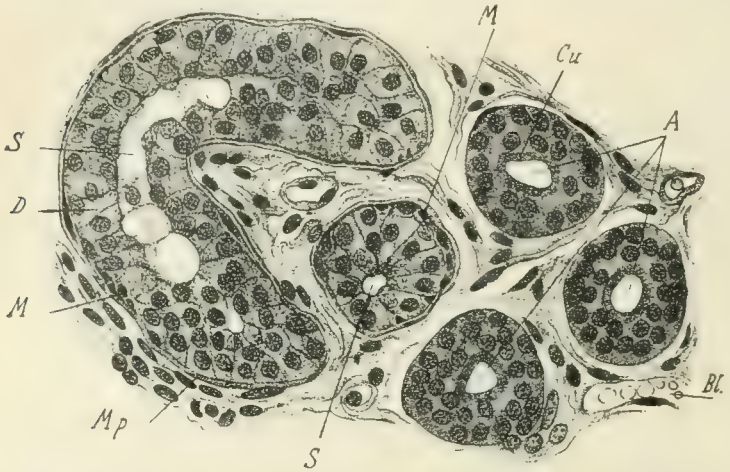


Fig. 5201.—Portion of a Sweat Gland from the Skin of the Back of the Foot. Magnified 400 diameters. (After Rabl.) *S*, Secreting portion of the coil; *D*, gland cells; *M*, smooth muscle fibres; *Mp*, membrana propria of the glandular tube; *A*, cross sections of the outlet portion of the gland; *Cu*, cuticula of the same; *Bl*, blood-vessel. Specimen hardened in a saturated aqueous solution of bichloride of mercury, and stained with hæmatoxylin and eosin.

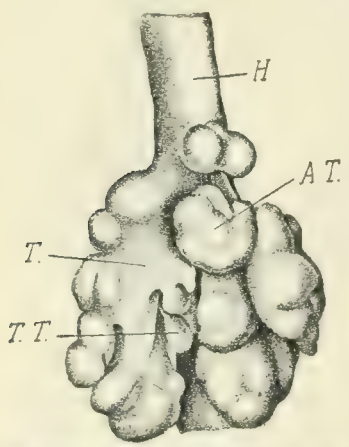


Fig. 5202. Model of a Group of Sebaceous Glands Surrounding a Hair of the Scalp. (After Rabl, from K. Bauer.) *H*, Hair follicle; *T*, sebaceous gland; *T.T.*, tubular gland; *A.T.*, alveolar gland.

The histological anatomy of the larger sweat glands, as has been already mentioned, differs somewhat from that of those just described. The differences are shown both in the coils and in the duct, by a dilatation and a narrowing of the canal in places. Where the lumen is larger there is only a single layer of epithelial cells; but in the narrower portions there are several. It is also claimed that muscle fibres are present in the former situations, but they are always absent from the latter.

The Sebaceous Glands.—*Embryology.*—The sebaceous glands of the skin make their appearance from the beginning of the fourth to the fifth month of pregnancy (Gegenbauer). Those glands which open directly upon the external surface of the skin, are formed from ingrowths of the rete Malpighii, which penetrate into the cutis. These epithelial prolongations are at first solid, but a canal soon forms in them by the fatty degeneration of the central cells. In its further development it is found that, by a process of cell proliferation, solid buds are given off from the original epithelial ingrowths, canals form in the axes of these, and the gland, finally consisting of several lobules, has become racemose. The origin of the sebaceous glands attached to the hairs is the same, except that the epithelial ingrowths proceed from the external root sheath of the hair. They appear very soon after the formation of the hair follicle by the prolongation of the rete into the cutis.

Distribution and Size.—The sebaceous glands are distributed very generally over the body, and are found everywhere in the skin, except upon the palms of the hands, the soles of the feet, and the last phalanges of the fingers and of the toes. They are particularly numerous upon the face and the scalp, where they are set very closely together. On the rest of the body they are found

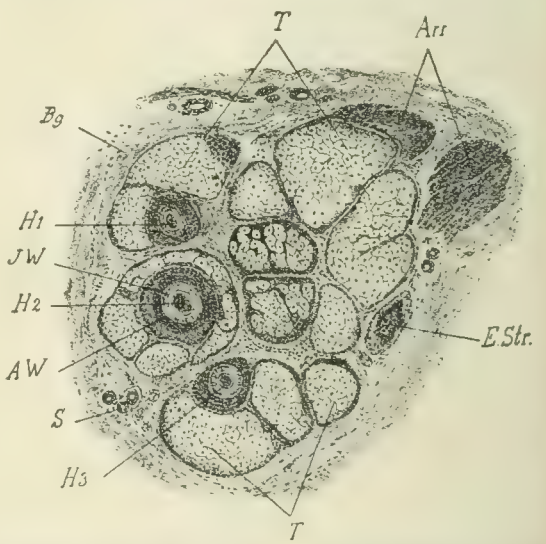


Fig. 5203. Cross Section of a Hair and Neighboring Parts at the Level of the Sebaceous Glands. The specimen, which had been taken from the scalp of an adult, was first hardened in Mueller's fluid and then stained with hæmatoxylin and eosin. Magnified 50 diameters. (After Rabl.) H_1, H_2, H_3, Cross sections of three hairs; *E.Str.*, a column of epithelial cells, constituting the connecting link between those which surround the hair bulbs (belonging to the hairs shown in the picture) and those lying above the papilla of a fourth hair; *T*, sebaceous glands belonging to the hairs shown in the cut; *J.W.*, inner root sheath; *A.W.*, outer root sheath; *Arr.*, arrector pili; *Bg*, connective tissue; *S*, sweat gland.

to be fewer in number and more widely separated. The glands vary very greatly in size. Of those connected with the hairs, the smallest are the ones on the scalp, 0.1 mm. to 0.16 mm. in diameter, but larger ones are attached to the hairs of the beard and axilla, from 0.16 mm. to 0.24 mm.; but the largest are on the mons veneris, the labia majora, and the scrotum. The sebaceous glands which are in connection with the lanugo hairs are from 0.25 mm. to 1 mm. in diameter. The length of the glands is from 40 to 160 μ, but the large ones on the nose measure even as much as 1 mm.

In shape there is also considerable variation. The simplest ones resemble small pouches, but the glands are usually found to be racemose or acinous, that is, composed of several lobules which possess one duct in common.

These glandular bodies are situated for the most part in the upper portion of the corium, above the level of the coils of the sweat glands. Some extend, however, through almost the entire thickness of the cutis.

They are found either directly attached to the hair follicles, into which their ducts open, at a variable distance from the orifice on the cutaneous surface, and empty the fatty matter secreted by them; or the external opening of their ducts is situated on the surface of the skin. These latter are the glands with which the lanugo hairs are associated. Besides these two forms, there are others which are entirely unconnected with hairs, and which also open directly upon the outer surface of the skin.

The sebaceous glands which open into the cavity of the hair follicles are the most numerous. They are seen wherever fully developed hairs exist, as on the scalp, the beard, etc. There is sometimes only one gland, but more often there are two, situated on opposite sides of the follicles, of different sizes, and at different heights. Their excretory ducts are short and pass obliquely upward to enter the follicles, the larger glands opening more superficially, the smaller ones more deeply, but the common location is at the junction of the upper and middle thirds.

The sebaceous glands which are associated with the lanugo hairs, and which open directly upon the external surface, are distributed over the forehead, cheeks, sides of the nose, and areola especially. They occur also more or less scattered over the trunk, the extremities, and the genitals. These glands are the largest, and also the most complicated in their structure. The duct is usually broad, and its orifice dilated. The hair attached to it is really an appendage, and passes through the duct to reach the outer surface of the skin. It has no follicle of its own, except at its deepest portion.

The glands which are in no way associated with hairs, and which open directly upon the external surface, are certain ones situated in special localities. They have received distinguishing names, and are known as the Meibomian glands in the eyelids, and the glands of Tyson on the glans penis and prepuce. To this class also belong the large glands of the labia minora, and those of the vermilion border of the lip.

Histological Anatomy.—A sebaceous gland may be considered to be composed of an outer wall and an inner mass of cells. The wall is formed of connective tissue, which is derived from the external sheath of the hair follicles; but in those glands which are associated with the rudimentary or lanugo hairs, and in those unconnected in any way with hairs, the fibrous envelope is obtained from the corium. The wall acts as a support (Morel) for a basement or membrana propria, which bears upon its inner surface a layer of cylindrical epithelial cells, and it also contains the nerves, blood-vessels, and lymphatics supplied to the glands. The membrana propria is exceedingly thin and amorphous. The single row of cells which are in connection with it is a continuation of the basic layer of the epidermis, the spiny cells stopping at the neck of the glands. The cavity of the glands is filled with large oval and polyhedral cells having large nuclei, but in the central portions there is a semifluid homogeneous mass, the sebum. The source of the sebum seen in the sebaceous glands are the cells, which are found presenting all stages of fatty degeneration. The most external ones are granular, the succeeding ones contain small drops of fat, which gradually increase in size as the central portion of the cavity is reached, until there is no trace of protoplasm remaining, the cell being completely filled with fat.

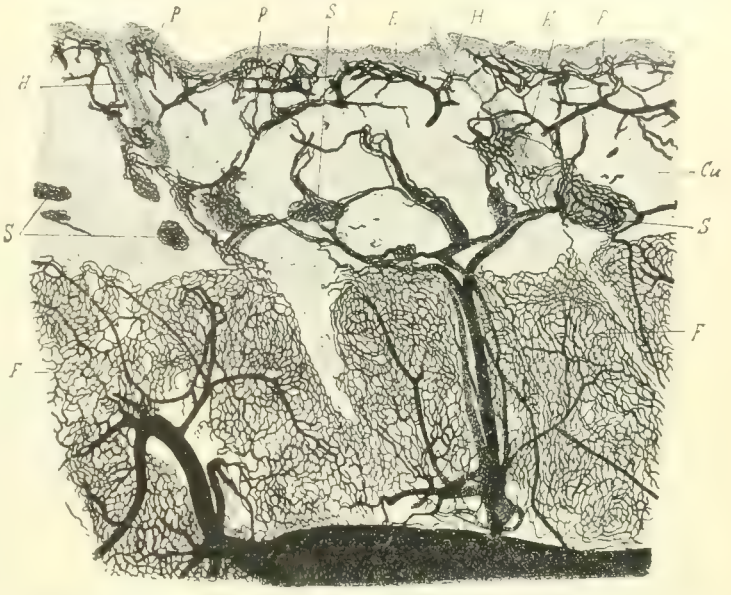


FIG. 5204. Section of the Skin of the Shoulder of a Child. The blood-vessels have been completely filled with gelatin colored with carmine. Magnified 40 diameters. (After Rabl.) *E*, Epidermis; *P*, papillæ; *Cu*, corium; *F*, subcutaneous fat tissue; *H*, shaft of hair; *K*, bulb of hair; *S*, coil of sweat gland. The specimen therefore shows, besides the larger trunks of blood-vessels, the capillaries belonging to the papillary layer, the sweat glands, parts of blood-vessels that supply the hairs and also those vessels which belong to the fat tissue. The large trunk of a blood-vessel seen at the lower margin of the picture is situated in the horizontal plane of connective tissue which serves to separate the subcutaneous fat tissue into two superposed layers. In the picture only the upper half of the panniculus adiposus is visible.

THE BLOOD-VESSELS OF THE SKIN.—The vessels which supply the skin with blood are branches from the larger arteries which lie below the subcutaneous fatty tissue. They pass up through this latter and form at its junction with the corium a more or less horizontal network. From this network further branches are given off, some to supply certain portions of the skin, others to ascend obliquely and perpendicularly through the cutis, having only few branches, until they reach the subpapillary layer of the corium. Here they again form a more or less horizontal network, which also gives off many branches.

The plexus of arteries at the junction of the cutis and subcutaneous tissue is very rich. It supplies the papillæ of the hair, the coils of the sweat glands, and also sends off branches which break up into capillaries in the panniculus adiposus. The subpapillary network of arteries supplies vessels to the external root sheath of the hair, the sebaceous glands, the unstriped muscles, and the ducts of the sweat glands. In addition, this plexus gives off branches which break up into capillaries just

below the papillæ, and into each of these a tortuous arterial capillary ascends almost to its upper end, where it forms a loop and goes over into a venous capillary. These latter unite to form venules in the same plane as

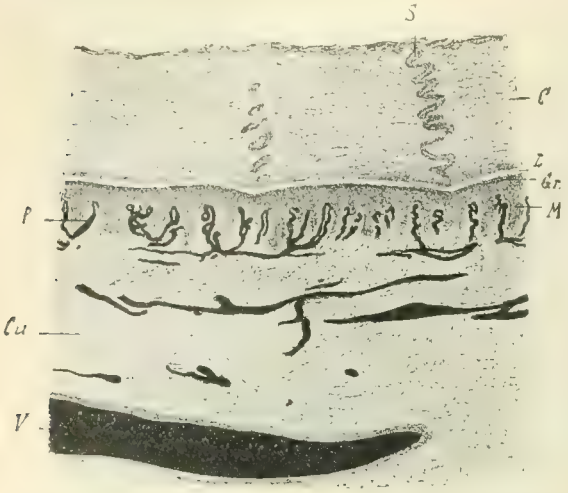


FIG. 5205. Section of the Skin of the Palm of the Hand. The cutting was done in a direction parallel to the ridges. The blood-vessels have been filled with gelatin colored by carmine. Magnified 50 diameters. (After Rabl.) *C*, Stratum corneum; *L*, stratum lucidum; *Gr*, stratum granulosum; *M*, stratum Malpighii; *P*, papillæ; *Cu*, corium; *V*, vein at the lower border of the corium; *S*, orifice of a sweat gland. Portions of the cutaneous plexus of blood-vessels and of the capillaries belonging to the papillæ are also shown in the picture.

the arteries, and course along them. When they arrive at the subcutaneous layer they, together with the veins from the other portions of the cutis, unite to form large venous trunks in the same plane as the large arteries. Between the two horizontal plexuses of arteries there is a portion of the cutis which has a very poor blood supply, and here even the bundles of fibres which go to form the pars reticularis do not receive any vessels.

FIG. 5206. Meissner's Tactile Corpuscle in a Papilla of the Tip of the Finger. The nerves have been stained by Fischer's gold method. (After Rabl, from Ruffini.) An afferent medullated nerve fibre enters the corpuscle from below and subdivides into a number of non-medullated varicose fibrillæ which traverse the corpuscle chiefly in a horizontal direction.

There are considerable differences in the distribution of the blood-vessels of the skin, and in the area supplied by any one branch. These areas are very small on the palms of the hands, the soles of the feet, and the face; also at the sulcus coronarius and the corona glandis, in which places each branch from the subpapillary arterial plexus, when it breaks up into capillaries, supplies only a few papillæ. The areas which are furnished with blood by one arterial branch are much larger in the greater part of the skin—the vessels breaking up into a number of capillaries—

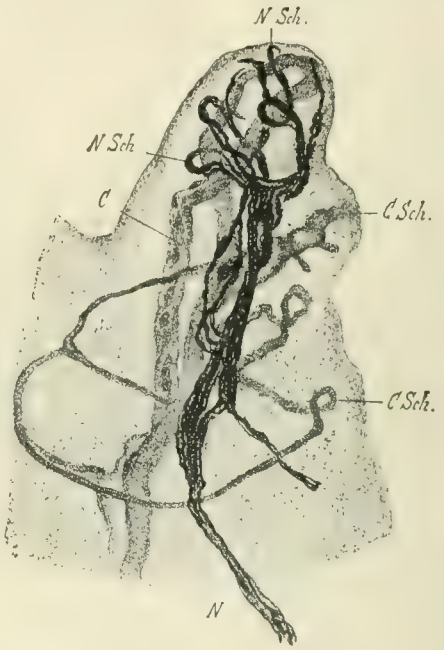


FIG. 5207.—Papilla from the Skin of the Tip of the Finger, showing Capillary Blood-vessels and Numerous Nerve Fibrillæ. Gold preparation. (From Rabl, after Ruffini.) *N*, Nerve trunk; *C.Sch.*, capillary loop; *N.Sch.*, nerve filaments surrounding the capillaries. (Greatly enlarged.)

and it is in general observed that they are more extensive on the extensor than on the flexor surfaces of the extremities.

Peculiar circulatory conditions are found in certain portions of the skin. On the ear, the alæ nasi, and in the region of the lips, large lacunæ are seen into which the venous capillaries empty from above, while from below the venules are given off. On the ends of the fingers there is likewise a special arrangement of the vessels. It has been found that here some branches of the digital arteries emptied directly into the large veins of the bed of the nails, without there being any intervening capillaries. Also it is observed that, after the vessels for the panniculus adiposus and sweat glands had been given off, but before the upper horizontal plexus for the supply of the papillæ

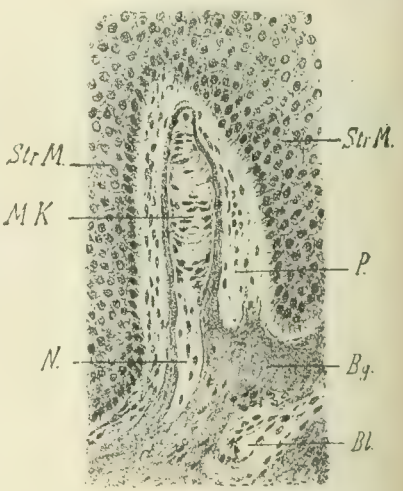


FIG. 5208.—Meissner's Tactile Corpuscle from the Skin of the Tip of an Adult Finger. Specimen hardened in alcohol and stained by means of hæmatoxylin and picrofuchsin. (After Rabl.) *MK*, Meissner's tactile corpuscle; *N.*, afferent nerve fibre; *P.* papilla; *Str.M.* stratum Malpighii; *Bg.*, connective tissue of the body of the papilla; *Bl*, blood-vessel.

had been formed, small arterial branches divided and broke up into many small coils. In the inner portion of these they emptied directly into venules.

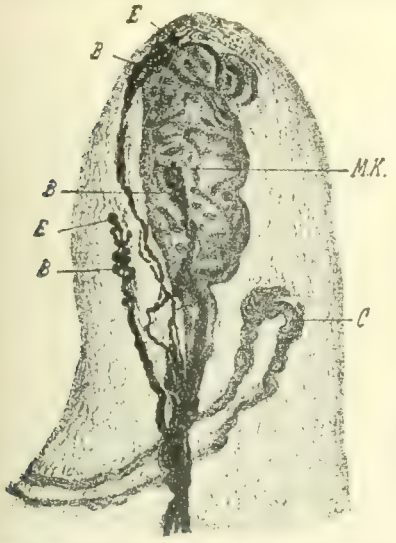


FIG. 5209. Papilla of the Skin of the Finger. Staining by Fischer's gold method. (After Rabl, from Ruffini.) The papilla contains, at its extremity, a Meissner's tactile corpuscle (*MK.*); farther down, a capillary loop (*C*), and on the left three independent, fascicular terminal plexuses of nerve fibrillæ (*B*); *E*, small terminal knobs of the nerve fibrillæ.

The lumen of the arteries of the skin is narrow, but that of the veins is large and wide. Their coats are slightly marked in the cutis, and they show only near the subcutaneous connective tissue an adventitia and a media. But even there these are poorly developed. All the vessels of the papillary layer of the corium are capillary in character, that is, simple endothelial tubes.

THE LYMPHATICS.—There are in the integument of the body two forms of channels which contain the lymphatic fluid, and through which it flows, viz., the lymphatic vessels proper, those which possess an endothelial lining, and the numerous spaces which occur between the elements composing the various layers of the skin.

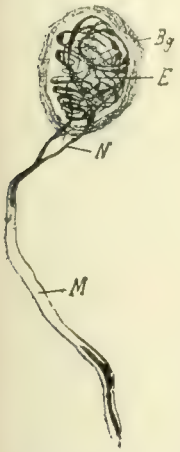


FIG. 5210.—Krause's Terminal Bulb from the Palpebral Conjunctiva. Nerves stained by means of methylene blue. (After Rabl, from Dogiel.) *M*, Afferent medullated nerve fibre; *N*, one of the non-medullated nerve fibrillæ resulting from the subdivision of the fibre *M*; *E*, terminal coil; *Bg*, connective-tissue capsule.

In regard to the latter, it has been proved that they are the origin of the lymphatic system of the skin, by the successful injection of the intercellular spaces in the spiny layer of the rete Malpighii from the lymphatics of the subcutaneous connective tissue (Retzius, Axel Key, et alii). Other lymph spaces exist between the membrana propria and the secreting cells of the coils of the sweat glands, and between the epithelial cells of the sweat ducts. The intercellular spaces in the stratum spinosum of the hair follicles and in the sebaceous glands are also points of origin for the lymphatics. The bundles of unstriped muscle fibres and the coils of the sweat glands and the bundles of connective-tissue fibres forming the cutis are sheathed by lymph spaces, as are also the fat clusters. According to Klein, very fine channels proceeding from these lymph sheaths penetrate into the latter and ramify betweeen all the fat cells of which they are composed.

The papillæ are also extensively traversed by lymph spaces, which empty into the lymphatic vessels proper. These vessels are lined with endothelium, and begin in the upper third of the papilla (the Hoggans) by means of a cul-de-sac. They course downward in the form of a plexus through the cutis, and at its junction with the subcutaneous connective tissue unite to form a few large vessels, which, according to Heming, have a muscular coat.

THE NERVES OF THE SKIN.—The nerves which are supplied to the skin are derived from branches of the cerebro-spinal system. They pass up through the subcutaneous connective tissue, in the same manner as the blood-vessels, from the larger trunks situated below. In the upper part of the panniculus adiposus the course of the nerves is a horizontal one, and they give off a large number of small branches for its innervation. They penetrate the cutis together with the arterial vessels, and accompany them more or less in their distribution. In their course they give off branches to supply the various constituent portions of the cutis. Those which supply the hair follicles pass to them in the neighborhood of the sebaceous glands, to which fibres are sent. They penetrate the hair sheath and are distributed between the cells of the root sheaths. The sweat glands

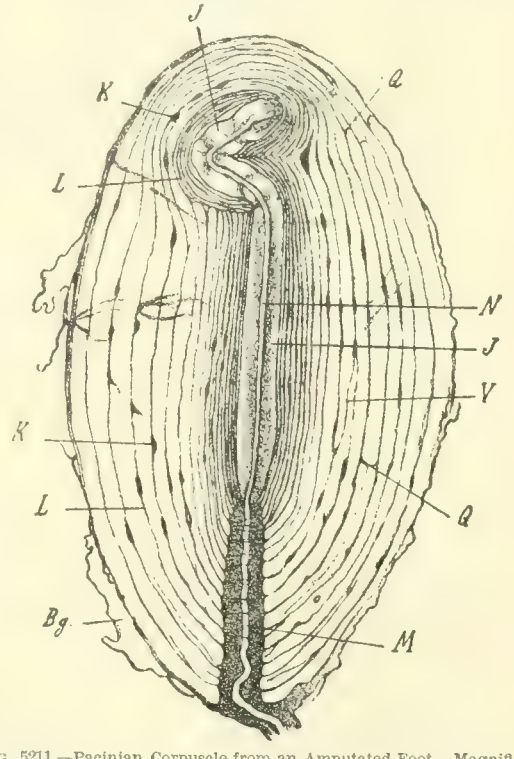


FIG. 5211.—Pacinian Corpuscle from an Amputated Foot. Magnified 70 diameters. (After Rabl, from Henle and Kölliker.) *M*, Medullated nerve fibre; *N*, non-medullated nerve fibre within the inner club-shaped sheath, *J*; *L*, lamellæ of the outer bulb-shaped envelope; *K*, nuclei of the connective-tissue cells; *V*, spot where two contiguous lamellæ unite, the lines of union forming an acute angle; *Q*, spot where the line of union runs transversely; *Bg*, connective tissue outside the corpuscle.

and their ducts are also furnished with nerves. Unna claims to have seen nerve endings between the secretory epithelial cells of the coils.

When the nerves arrive at the upper portion of the cutis they take a horizontal course and form a rich plexus just below the epidermis, which gives off a great number of branches. These break up into fine fibrillæ, and are distributed in every direction. These fibrillæ terminate either in the endothelium of the papillary blood-vessels, or free in the connective tissue of the papillary body, or penetrate into the interepithelial spaces of the stratum spinosum. Longer branches from this plexus ascend into the papillæ, and in certain portions of the integument end in the tactile corpuscles.

The nerve fibres which, it is claimed, have been traced between the cells of the epidermis are non-medullated.

They are said to be distributed generally throughout the rete Malpighii, as far up as the stratum granulosum, and to end in the intercellular spaces, either tapering to a

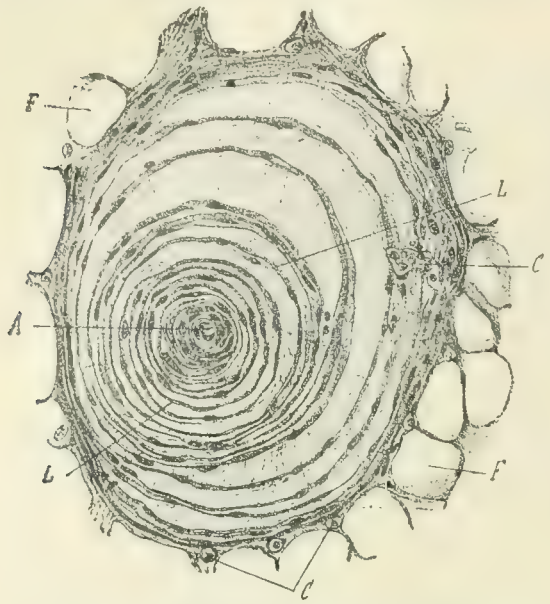


FIG. 5212.—Transverse Section of a Pacinian Corpuscle, from the Skin in the Neighborhood of the Anus. Specimen hardened in a solution of picrin and bichloride of mercury and stained with hæmatoxylin and eosin. Magnified 200 diameters. (After Rabl.) *A*, Axis cylinder lying in a narrow, circular, perfectly clear space, the inner club-shaped sheath; *L*, lamellæ of the outer capsule or envelope; *C*, capillaries; *F*, fat cells.

point or with a small rounded extremity. Unna claimed that they terminated in small discs upon the cells, but his view has not received recognition.

Besides the above-mentioned ways in which the nerves end in the skin, there are special forms of termination. These are represented by the tactile corpuscles, the tactile discs of Ranvier, the Pacinian bodies, and the end bulbs of Krause.

Tactile Corpuscles.—The tactile corpuscles are very small, oblong bodies from 40 to 200 μ in length, and from 30 to 60 μ in breadth. They are situated in the upper portion of a broad papilla, and are found especially on the fingers and toes, and in the palm of the hand. They have a distinctly striated appearance, and are directly connected with one or two medullated nerve fibres which wind around the corpuscle, and, on entering it, lose their medullary sheath, the perineurium becoming continuous with the capsule of the corpuscle. The nerves split up into branches, which end in flattened knobs between the connective-tissue cells of which the corpuscle is composed. They often consist of two or three sections lying close together, each one being supplied with a nerve.

Ranvier's Tactile Discs.—These discs are small cup-shaped bodies, the concave side of which is always directed toward the free surface of the epidermis. At several points on the convexity of the disc the termination of a non-medullated nerve fibre is seen. Ranvier claims that this nerve ends only on the surface of these discs, but according to others this takes place in the cell between the nucleus and the external membrane. This form of nerve ending has been found in the deeper portions of the epidermis, near the sweat duct, and in the corium just below the rete.

The Pacinian Bodies.—The Pacinian bodies were first thoroughly described by Pacinius, though they had already been mentioned by Vater over a hundred years ago. They are small, oval, transparent bodies from 2 to 3 mm. long and 1 to 2 mm. broad, and are situated in the subcutaneous connective tissue, almost exclusively upon the branches of the nerves which supply the skin of the palms of the hands and of the soles of the feet, but also upon the dorsal nerve of the penis and of the clitoris. They are likewise found in other places, as around the joints, where they are deeply situated, and also in the mesentery, etc. The major part of the Pacinian body is formed by the capsule. This capsule is derived from the perineurium of the nerve, which ends in the corpuscle, and is in reality composed of a large number of concentrically arranged laminæ, which are separated one from the other by a layer of flat endothelial cells. Between any two of these there is a more or less large quantity of an albuminous fluid, and connective-tissue fibres forming septa are also seen. This laminated and concentrically arranged capsule surrounds a narrow cylindrical space, which contains a granular substance in which a few cells are seen, and the termination of the nerve fibre. At its entrance into the cavity of the Pacinian body, the nerve loses its medullated character and the axis cylinder alone passes in. It appears as a pale, finely granular, narrow band, which ends in a single small knob or in a series of them. The nerve has also been observed to pass entirely through one of these bodies and end in another. A small artery penetrates the capsule of the Pacinian bodies along with the nerve, and forms a capillary plexus between the peripheral laminæ.

End Bulbs of Krause.—The end bulbs of Krause are minute oval or cylindrical bodies, which are regarded as being more or less related to the tactile corpuscles. They consist of a connective-tissue capsule containing a large number of cells which form a core. Between these, one or more nerve fibres end. They are found in the conjunctiva and the mucous membranes of the mouth, the glans penis, clitoris, and vagina, where they are termed genital corpuscles. The capsule of these end bulbs is derived from the perineurium, but the nature of the core which it contains is still a mooted point. The axis cylinder alone penetrates into this core, having lost its medulla, and it ends in the upper portions either free or as a small button-like protuberance.

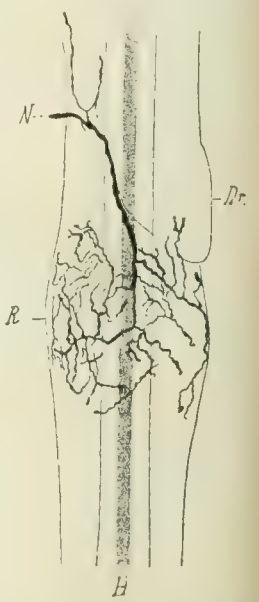


FIG. 5213.—Hair from the Lip of a Human Embryo 19.5 cm. long. (After Rabl, from G. Retzius.) *N*, Afferent nerve fibre, which first gives off a small forked branch in an upward direction, and then subdivides into a ring-like plexus (*R*) completely surrounding the outer sheath of the hair root which at this point is somewhat thickened. This plexus consists of a few nearly horizontal fibrillæ between which run numerous vertical ones; *Dr*, sebaceous gland.

THE APPENDAGES OF THE SKIN.

THE NAILS.—*Embryology.*—The first steps in the development of the nails occur in the third month of fœtal life, and consist in the marking out of the nail bed and furrow. This is covered by the ordinary stratum corneum of that period of life, and it represents the eponychium of Unna. Underneath the eponychium the embryonic nail remains up to the fifth month. According to Kölliker, there appears in the fourth month, between the eponychium and the stratum mucosum, a layer of large, pale-colored, horny plates, which cover the bed of the nail and represent its primary form. The nail in its further growth increases in thickness quite rapidly, possesses a free border by the sixth month, and by the seventh month is fully formed. Kölliker also claims that the development of the nail takes place from

the entire nail bed, but Unna insists that he has observed the formation of a germinal spot in the matrix from which the embryonic nail grows and pushes itself forward beneath the eponychium.

General Characteristics.—The nails of human beings are elastic structures of a horny texture situated upon the dorsum of the last phalanges of the fingers and of the toes. Each one is convex upon its external surface, concave upon its internal and moulded upon the cutis, to which it is firmly adherent. The exposed portion of the nail is called its body; the anterior extremity, the free edge; the semilunar portion posteriorly, which is of a white opaque color, the lunula. The portion of the cutis upon which the nail is situated is the nail bed. It is bounded laterally by two rolls of the skin, which are known as the walls of the nail. Around the nail bed is a groove which is covered by the nail wall, and in this lie the lateral edges of the nail, while the posterior portion, the nail root, is implanted in a similar though much deeper groove; this latter represents the matrix, and it is from here that the growth of the nail takes place.

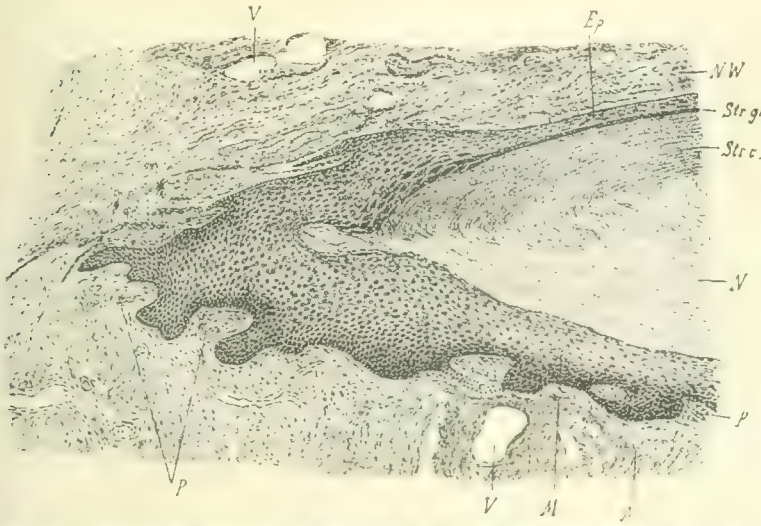


FIG. 5214. Longitudinal Section of the Bed of the Nail, Near its Posterior End of the Root of the Nail. The entire specimen was dissected free from the bone at point of toe. Alcohol was used for hardening the tissues and picro-acid and picro-fuchsin for coloring them. Magnified 50 diameters. (After Rabl.) *NW*, Wall of the nail; *Ep*, eponychium; *Str gr*, stratum granulosum; *Str c.*, stratum corneum, colored reddish-yellow by means of picro-fuchsin; *N*, nail, colored yellow; *M*, matrix of the nail; *P*, papilla; *V*, vein of the corium beneath the matrix.

Histological Anatomy.—The bed of the nail consists of the corium and the stratum mucosum. The connective-tissue bundles of the cutis run here partly longitudinally and parallel to the axis of the fingers, partly in a perpendicular direction from the periosteum to the external surface. The epithelium covering the corium is composed of cells identical with those in the stratum mucosum of the epidermis, and is sharply defined from the nail, except at the matrix.

The corium at the matrix of the nail shows a well-developed papillary body, and is very vascular, each papilla receiving a blood-vessel. In front of this and beneath the lunula the papillæ are very small, and still more so anteriorly; the cutis forming the nail bed has no papillæ but fine longitudinal ridges, in which run the blood-vessels, which give off capillary branches at regular intervals. These ridges of the corium are covered by the epithelial cells of the stratum mucosum, which also dips down between them.

The nail itself consists of horny lamellæ, which are closely bound together, and which are composed of cells similar to those of the epidermis, except that they contain nuclei.

In the formation of the nail the matrix plays the important part, and it is from this portion that regeneration of the nail is continually going on.

THE HAIRS.—*Embryology.*—The first steps in the development of the hairs occur at the end of the third or the beginning of the fourth month of fœtal life. They are shown by the formation of small, solid prolongations of the rete Malpighii, penetrating into the cutis and increasing in length by the proliferation of the cells composing them. Arriving in the deeper portion of the cutis, the lower end of the prolongations is very soon surrounded by an aggregation of round and spindle cells, which partly form the papilla of the hair and partly grow around the epithelial ingrowth in order to form the sheath of the hair follicle (Unna). During this time changes also take place in the epithelial column. In its inner portion a conical-shaped mass of cells, with its apex directed externally, becomes differentiated from the remainder, and this represents the primitive hair body. From it the hair and its inner root sheath are formed. The primitive hair body having grown around the newly formed papilla, it increases in length upward and keratofication begins and proceeds from above downward. The external root sheath is constituted by the portions of the epithelial ingrowth of the rete Malpighii which remain after the differentiation of the primitive hair body and surround the entire hair.

From the sixth to the eighth month of life the fœtus has become covered with hair, which, however, falls out and is replaced by new hair. This regeneration of the hair on the fœtus is continuous as in adults, but the

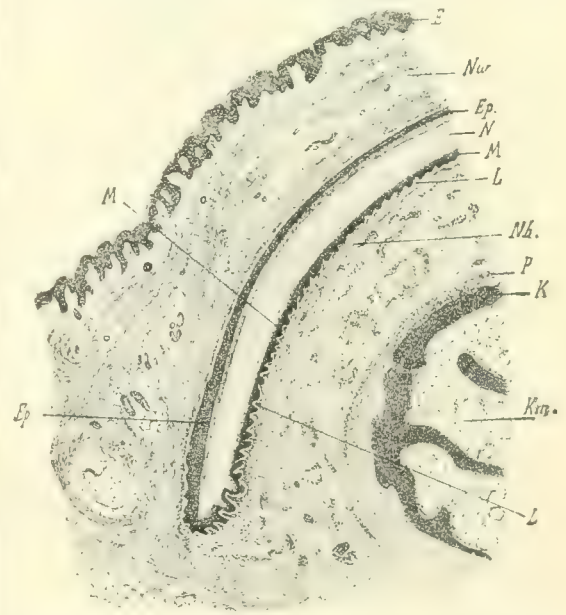


FIG. 5215.—Cross Section of the Basal Portion of the Nail of an Adult. Specimen hardened in Mueller's fluid and stained with hæmatoxylin and eosin. Magnified 25 diameters. (After Rabl.) *E*, Epidermis of the wall of the nail (*Nw.*); *Ep*, eponychium; *N*, nail; *M*, matrix of the nail; *L*, longitudinal border of the matrix; *Nb.*, bed of the nail; *P*, periosteum; *K*, bone; *Km.*, bone marrow.

rapidity of the change ceases a few weeks after birth. The embryonic or lanugo hairs, which have a much shorter length of life than those which grow after birth, give place to more permanent ones, and on certain por-

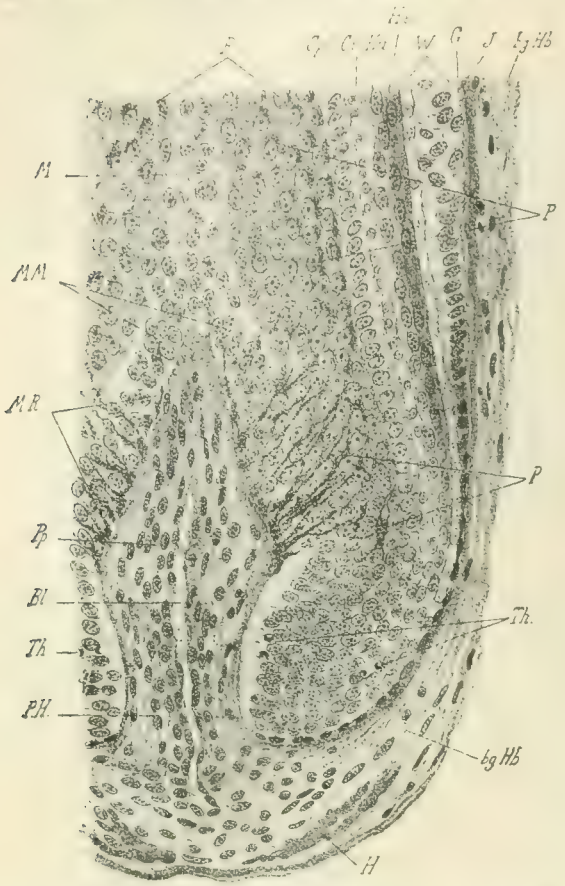


FIG. 5116. Longitudinal Section of a Papilla, a Hair Bulb, and the Lowest Part of the Shaft of the Hair with its Sheaths, from the Scalp of an Adult. Magnified 300 diameters. (After Rabl.) *Pp.*, Papilla; *P.H.*, neck of the papilla; *Bl.*, blood-vessel; *M.*, cells of the medulla of the hair; *R*, cortical cells; *MM.*, matrix cells of the medulla; *MR.*, matrix cells of the cortex; *Th.*, cells undergoing karyokinesis; *P*, pigment; *Cu*, membranous envelope of the hair; *Cr.*, membranous envelope of the root-sheath; *Hu*, Huxley's layer; *He*, Henle's layer; *W*, outer root sheath; *G*, vitreous membrane; *J*, innermost layers of the connective-tissue hair follicle (*bg Hb.*); *H*, kollastin.

tions of the body acquire a much greater development than they do on others. The new hairs originate from the epithelium forming the external root sheath of the lanugo hairs, which sends out solid buds from which the hair develops in exactly the same way as has just been described, and grows up alongside of the embryonic hair to the external opening of the follicle. The old hair has, in the mean time, been separated from the papilla and become completely horny, owing to its loss of nourishment, and, being pushed upward by the new-formed hair, falls out when the external surface is reached. In this way the temporary hairs are replaced by the permanent ones, and an entirely similar procedure is furthermore constantly seen repeating itself, even in adults.

General Characteristics.—The hairs, which are modifications of the epidermis, are found in greater or less amount over the entire body, with the exception of the palms of the hands, the soles of the feet, the vermilion border of the lips, the glans penis, the labia minora, and inner surface of the labia majora. Over the majority of the surface they are short, rather colorless, having the character of the embryonic hairs, and hence are termed the lanugo hairs; but on the head, the eyebrows and the eyelids, in the axillæ, on the pubes, and in the male sex on the cheek and upper lip, they attain a much higher grade of development.

The hairs which are present upon the scalp, eyebrows, and eyelids become gradually more marked, thicker, and longer after birth, but at the age of puberty the hairs on the pubes and in the axilla, and the beard in the male, begin to develop and to increase rapidly. Hair also is found around the anus in the male. It is not unusual to see, in certain races, that in women, as they approach and pass the climacteric, a stronger growth of hair appears on the upper lip and face.

The hairs, both the lanugo and the fully developed ones, are for the most part placed obliquely in the skin and are situated in follicles termed the hair follicles. These latter are sometimes short, the papilla lying high up, or, again, of considerable length, and deep down in the subcutaneous connective tissue. The portion of the hair situated in the follicle is the root, that above the level of the skin, the shaft. At the lower extremity of the root there is a whitish, soft, bulbous enlargement, the hair bulb, which has a concave end that fits upon the conical vascular eminence already mentioned as being the hair papilla.

The hair follicle itself may be divided into three parts, according to its form. From its upper extremity, where it opens out upon the surface of the skin, it descends, shaped like a funnel, as far down as the opening of the duct of the sebaceous gland. It then becomes narrowed for a short distance, but broadens again near the papilla to receive the hair bulb.

The hair shaft varies considerably in shape, being in some cases round, in others much flattened, or again angular.

On cross section the hairs are either round, or oval, or triangular, or square, having convex or concave sides.

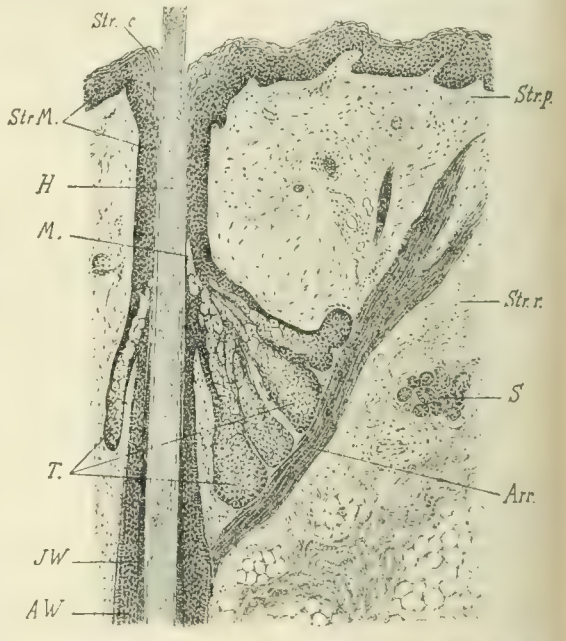


FIG. 5217.—Hair of an Adult at its Point of Emergence from the Scalp. Specimen hardened in Mueller's fluid and stained with hæmatoxylin and eosin. Magnified 50 diameters. (After Rabl.) *H*, Shaft of hair; *J.W.*, inner sheath of root of hair; *A.W.*, outer sheath of root; *T*, sebaceous gland; *M*, outlet of this gland; *Arr.*, arrector pili; *Str.c.*, stratum corneum; *Str.M.*, stratum Malpighii; *Str.p.*, stratum papillare corii; *S*, sweat gland.

The angular and flattened hairs are found in those localities where the hair is curly, the round ones where it is straight.

At its free external end the hair is pointed when in its natural state, but owing to the fact that it is continually subjected to mechanical influences, such as rubbing, etc., it is usually found to have a more or less rounded extremity.

Histology of the Hair and of its Follicle.—Hair Follicle.—The hair follicle is represented by a sac-shaped cavity composed of connective tissue. At its lower end, which is more or less deeply situated in the cutis, an eminence is seen, analogous to the papillæ in the upper portion of the corium, which is known as the hair papilla. This body, upon which the concave extremity of the hair root is accurately fitted, is oval in shape, and at its base is a distinctly marked constriction—the neck of the papilla. It is composed of connective tissue, similar to that of the cutis, of which it is a part, and contains blood-vessels. (See also Fig. 5203.)

The hair follicle envelops the lower two-thirds of the hair and of its sheaths, but above the openings of the ducts of the sebaceous follicles it is not demonstrable as a separate formation, becoming lost in the tissue composing the papillary body. It consists of three coats. The most external of these is a portion of the cutis proper, and is composed of connective-tissue fibres, which are closely bound together and run longitudinally in the axis of the hair, and is quite rich in connective-tissue cells. In it are distributed the blood-vessels and nerves supplied to the hair. The next innermost coat is composed of elements similar to those which are found in the most external, but they are arranged in a circular manner running around the hair follicle. There are many nuclei found in this coat, the long axes of which are directed parallel with the course of the fibres, and they resemble very strongly the nuclei seen in unstriped muscles; but this resemblance is in all probability due to the tension to which the fibres are subjected.

The innermost of the coats of the hair follicle is a hyaline basement membrane, which has a glassy, transparent appearance. It is in immediate contact with the cylindrical layer of epithelial cells belonging to the external root sheath of the hair. It is not always demonstrable, varying greatly in thickness, and is most clearly marked in the lower third of strongly developed hairs. In the lanugo hairs the connective-tissue envelope of the hair is absent, the root sheaths being derived from the epidermis forming the hair follicle.

The Hair Sheaths.—The root of the hair proper is in the greater portion of its extent covered by an envelope, which consists of several layers of cells very adherent to it. It constitutes the inner root sheath of the hair, and lies in contact with the external root sheath, by which it is separated from the connective-tissue envelope of the hair follicle.

The Hair Proper.—When a fully developed hair is examined under the microscope, it can be seen that it is composed of three tissues, which differ from each other in appearance. These three portions are termed the cuticula, the cortex, and the medulla. Each of these can be easily recognized in the shaft of the hair, but not so readily at the bulb. Still, if the hair is treated with picrocarmine, the cuticula can be traced here, and it can be seen that it starts from the neck of the hair papilla (Unna). By the same method, it is also found that the cortex develops from the lateral portions of the papilla, and the medulla from the apex.

The Cortex.—The most voluminous portion of the shaft of the hair is constituted by the cortex, a transparent fibrillar mass of varying color. In it are seen dark spots and longitudinal streaks, which are situated between the horny elements of the hair, and are caused by the presence of air. Pigment granules are also present in greater or lesser quantities.

When the hair is treated with sulphuric acid the cortex breaks up into the fibres of which it is composed, and, if the action of the acid has been long continued, it may even separate into long, narrow, spindle-shaped plates. In the centres of these latter an indistinct linear figure is oftentimes traceable. It represents the remains of the nucleus of the cell from which the plate was derived.

The development of the hair from cells is very distinctly seen at the papilla. The portion of the hair in immediate contact with this body is hollowed out or concave in shape, and it is composed of a row of cylindrical epithelial cells entirely similar to those forming the basic

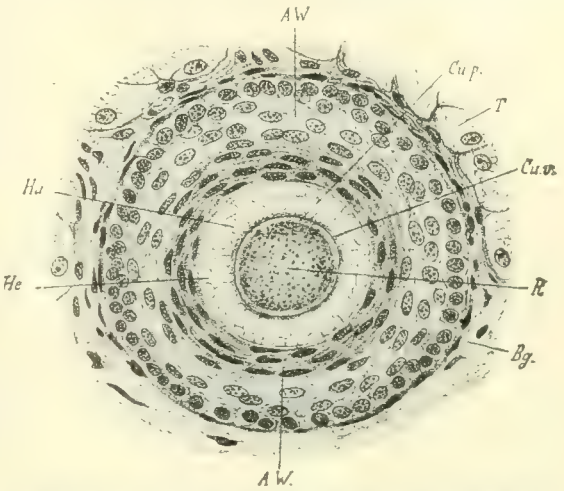


FIG. 5218. Cross Section of a Hair and its Sheath, from the Scalp. Specimen hardened in Mueller's fluid and stained with hæmatoxylin and eosin. The cut was made at the level of the region in which lie the sebaceous glands. Magnified 250 diameters. (After Rabl.) *R*, Cortical portion of the hair shaft (the medullary substance is lacking in this specimen); *Cu.p.*, cuticula of the hair; *Cu.r.*, cuticula of the sheath of the root; *Hu*, Huxley's layer; *He*, Henle's layer; *A.W.*, outer sheath of the root; *Bg.*, connective tissue; *T*, sebaceous glands.

layer of the epidermis. This layer of cells is termed the matrix of the hair, and it is upon it that the growth of the hair depends. Starting from this point, it can also be seen how the cells and their nuclei grow longer, become finely fibrillated and granular, and finally, when entirely horny, appear as small plates. These successive changes should be studied on hairs which are little pigmented, for in them they can be seen much more easily than when the opposite is the case. The cells of which the cortex of the hair root is formed have been found by Waldeyer to be composed of small fibres. Each cell is united to the contiguous ones by short spines, in a manner analogous to the cells composing the epidermis.

The pigment which gives the hair its various shades of color is an important constituent of the cortex. It varies greatly in quantity, and in proportion to its abundance or comparative absence the hair is dark or light in color. It occurs both in a diffuse form and also in granules. The elements of the cortex are diffusely pigmented by the former, but the pigment granules are distributed here and there, and are situated in and between the cells composing the cortex (Waldeyer). This deposition of the pigment granules in the cells is most clearly seen in the root of the hair. The source of the pigment is not yet fully established, though Riehl and others more lately have thrown some light on the subject. In the tissue of the papilla of the hair irregular-shaped nucleated cells, the protoplasma of which contains a considerable amount of pigment, have been found. They were present as far up as the matrix of the hair, between the cells of which they sent long prolongations, and they could also be traced higher up as fine intercellular pigment deposits. Riehl also observed that the cells of this portion of the hair root, which were not yet horny, contained granules of pigment around their nuclei, and also that the cells of the matrix were quite closely connected with the prolongations of the wandering pigment cells of the hair papilla, from which their protoplasm took up pigment granules. In regard to the source of these

granules, Riehl argued that, inasmuch as wandering pigment cells were regularly met with in the papilla of the hair and following the course of the blood-vessels, the blood must be the source of the pigment, and this latter must be carried by the cells to the hair.

The Medulla.—The medulla is situated in the axis of the hair throughout almost its entire length, but it narrows and terminates at some distance from the free end. It is marked in the stronger hairs, but is usually absent in the lanugo hairs, and often also in those of the scalp. The presence of the medulla is shown by a more or less broad, longitudinal band of a dark color, which is due to the air situated between its composing elements. These latter are cells which are shrunken into irregular shapes, possess no nuclei, and are furnished with spines and prongs (Waldeyer).

At the bulb of the hair, the medulla differs very slightly from the cortex. Over the apex of the papilla and above the cylindrical cells situated there, which represent the matrix of the medulla, large nucleated cells are seen, and in their protoplasm are large drops of keratohyalin. In proportion as the shaft is ascended, these cells become shrunken, harder, lose their nuclei, and the keratohyalin disappears. They are bound together by means of the spines and prongs on their surface, between which are left spaces—intercellular spaces. Below the external surface these spaces serve as channels through which nourishment is furnished to the young cells of the medulla, but where the hair is exposed to the external atmosphere this fluid evaporates, and the spaces become filled with air.

The Cuticula.—The hair is also furnished with a cuticula, which surrounds the greater part of that portion of the hair which lies in the follicle. It is formed by a layer of horny plates, arranged like tiles on a roof, and they are closely bound together. The cuticula originates from the neck of the papilla of the hair, between the matrix of the cortex and that of the inner root sheath. At this point it consists of several rows of cylindrical nucleated cells, which divide soon after leaving the matrix into two layers. One of these goes to form the cuticula of the hair, the other the cuticula of the inner root sheath. The cells of the former are at the middle of the hair papilla, directed perpendicularly to the circumference of the hair, but gradually become more and more inclined toward it. At the upper portion of the hair follicle the cuticula is no longer distinguishable and becomes a constituent portion of the cortex. At the matrix the cells are epithelial in character, but they become transformed into solid transparent horn plates without nuclei.

The Root Sheaths.—The hair root is further enveloped by two coats—the root sheaths—which are closely adherent to it. They are known individually as the inner and the outer root sheath. The former is immediately around and in contact with the hair, and ends within the hair follicle; the latter, more external, passes up to the orifice of the follicle, where it becomes continuous with the spiny layer of the epidermis.

The Inner Root Sheath.—The inner root sheath is composed of three layers—the cuticula, the one nearest the hair, Henle's layer, the most external, and between these two Huxley's layer.

The cuticula of the inner root sheath arises from the same matrix at the neck of the hair papilla as the cuticula of the hair. The cells composing it are so arranged that their long axes are parallel to the circumference of the hair, that is, in an opposite direction to the cells forming the cuticula of the cortex. They undergo transformation in a manner entirely analogous to the one which has been already described for the cuticula of the cortex. The cuticula of the inner root sheath is lost sight of within the follicle, becoming a part of the sheath.

The Layers of Huxley and of Henle.—The portion of the inner root sheath which is situated between the cuticula just described and the external root sheath is composed of the two layers known as those of Huxley and of Henle. They also take their origin from the neck of the papilla, and at that point appear as a layer of three or more cylindrical epithelial cells. Drops of keratohyalin, however, appear very soon in these cells, and this substance increases rapidly in quantity. The change in their appearance due to the presence of the keratohyalin is very marked on a level with the apex of the papilla, and the cells are seen here to have attained a much larger size. The cells forming the layer of Henle—the most external—contain, however, a greater amount of keratohyalin, and undergo hornification much more rapidly than they do in the layer of Huxley. Consequently, Henle's layer is found represented by horny, polygonal, non-nucleated elements at a much lower level than Huxley's layer. This latter, the inner portion of the inner root sheath of the hair, is composed at the papilla of cells which contain a smaller amount of keratohyalin. Keratofication in them is not so rapid as in the cells of Henle's layer, the nuclei do not disappear so early, and the complete transformation of the elements of Huxley's layer into horny masses occurs at a higher level than is seen in the former one. The inner root sheath ends in the hair follicle.

The External Root Sheath.—In describing the embryology of the hair, it was stated that the first changes observed consisted in a proliferation and prolongation downward into the cutis of a portion of the cells forming the stratum spinosum of the epidermis. The further steps which occurred in the evolution of the hair, and which took place in the central portion alone of this prolongation, it has also been seen, resulted in the formation of the shaft of the hair, but the remaining portion also serves an important purpose. It represents the external root sheath, or envelope, of the hair, and is separated by it from the connective tissue composing the follicle.

The outer root sheath is not uniform throughout its entire extent, but is lined on the surface next to the hair shaft, and as far down as the opening of the duct of the sebaceous gland, by the stratum corneum and stratum granulosum. From here to the level of the hair papilla the stratum spinosum descends in its entirety, but then narrows, and at the neck of the papilla is reduced to a layer of two or three cylindrical cells. It lies at this point in close contact with the cells from which the inner root sheath is formed.

The appendages of the hairs are the sebaceous glands, and bundles of unstriped muscular fibres are also attached to them. They have been, however, already described.

George T. Elliot.

SNAILS.—A popular term applied to those forms of the gasteropod mollusks, belonging chiefly to the order *Pulmonata*, which are provided with a shell. They are divided into the land, fresh-water, and marine species, belonging respectively to the suborders *Geophila*, *Limnophila*, and *Thalassophila*. There are some few terrestrial species and a large number of fresh-water and marine forms, belonging to the order *Azygobranchia*, to which the term snail is also sometimes applied. The fresh-water and marine forms are perhaps more commonly known as periwinkles and whelks, while allied genera not provided with a shell are ordinarily spoken of as slugs.

The order *Pulmonata* is characterized by a lingual membrane provided with numerous teeth arranged in many uniform transverse rows; mouth usually supplied with one or more horny jaws, a respiratory organ in the form of a closed chamber lined with pulmonic vessels on the back of the animal and covered by the shell when present; the edge of the mantle being attached, and the entrance to the air chamber being through an opening in the side closed by a valve. The operculum is almost universally absent. The tentacles and eye peduncles are retractile or contractile. The shell varies in form, and is sometimes rudimentary or wanting. They are hermaphrodites, with reciprocal impregnation, generally oviparous, and all forms, whether terrestrial, fluviatile, or marine, respire free air.

The American species of terrestrial snails live mostly in the forest sheltered under the trunks of fallen trees.

layers of decayed leaves, stones, or in the soil itself. They are, as a rule, solitary in their habits; only exceptionally, as sometimes in the early days of spring, do they congregate in considerable numbers in warm and

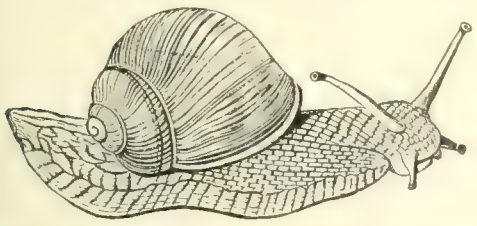


FIG. 5219.—Helix Pomatia Linn.; the European Vineyard Snail, the one most extensively eaten. (From Keferstein.)

sunny situations, but these assemblies do not last more than a few days; they then scatter and again resume for the rest of the year their solitary mode of living. They are rarely seen abroad except on damp dark days or at twilight, and, indeed, they almost disappear as the forests are cut down, and seem to flee the approach of man. The European species, on the other hand, follow in the track of cultivation and are common in gardens and fields, on walls and hedges, and other places exposed to the action of light. It is probably owing to this radical difference in their habits of life that the large majority of our species are so plain and uniformly dull-colored, while the European species are brightly colored. In size the snails vary from those minute species a quarter of an inch or less in length to the gigantic African species belonging to the genera Achatina and Balinus, which sometimes attain the length of eight inches.

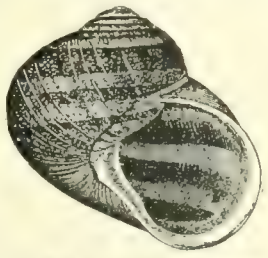


FIG. 5220.—Pomatia Aspersa. (From Binney.)

The eggs are laid in the early spring. Some few forms are viviparous. As soon as hatched, which takes place in from twenty to thirty days, the young snail devotes himself strictly to the business of eating. He first devours his own shell, and then, according as his instinct leads him, begins on either vegetable or animal food. The majority of them prefer vegetable food, though it is certain that some forms are also fond of animal food, and sometimes prey upon earthworms, their own eggs, or even upon each other. The amount they can eat is enormous, as can well be testified to by the gardener, who often finds a whole field of vegetables almost destroyed in a single night. As might be expected from this, their rate of growth is very rapid, and they frequently double in size within a week. At the first approach of frost they retire into secluded and sheltered spots under logs or stones, or partially burrow into the soil, withdraw into their shells, and dispose themselves for their annual sleep or hibernation, only to be awakened again in from four to six months by the warmth of spring.

They possess the power of secreting a mucus-like material from the general surface of the body at will. The slugs have this function developed to a much greater degree, and it is used by them as a means of defence. Whenever a foreign substance touches them they secrete a quantity of the mucus, which forms a kind of membrane interposed between themselves and the irritating substance. This mucoid material is a non-conductor of heat and impervious for a time to liquids, so that by its means they are enabled for a considerable time to withstand the action of corrosive gases, alcohol, and even boiling water. The fresh-water and marine forms live on the rocks and aquatic plants at the bottoms of ponds and rivers, and along the seashore, where they may be seen in immense numbers when at any time, as at ebb-tide, the rocks are exposed.

There are a large number of species of snails which have been used as food. Most of these belong to the genus Helix, of which more than twelve hundred species have been described. Few of the American forms have been so used, partly for the reason that it has never become the custom here, and partly, probably, from the curious fact, already mentioned, that the forms indigenous to this country are mostly solitary and do not collect in herds or communities. Many of the European species, on the contrary, herd together in immense numbers and so are very easy to collect and peculiarly adapted to colonization. The "edible snail," *Helix pomatia*, is the one most commonly eaten in Europe, but *H. aspersa* and *H. hortensis* are also very generally used. The first of these has, I believe, never been introduced into this country, but *aspersa* and *hortensis* both have been, and are now found in considerable numbers in certain localities. They retain their habits of congregation, and will no doubt in time be much more generally used as an article of diet than they are at present.

The ancient Greeks and Romans regarded snails as one of their greatest delicacies, and imported them from all parts of the then known world to be reared and fattened in their extensive snail ponds. In many parts of Africa the large species which are indigenous there are used as a daily food all the year round. At the present time in Austria, France, Switzerland, Spain, and Italy, the collection, rearing, and preparing them for market afford occupation to a large number of people. An idea of the extent of the industry may be gained from the fact that from Ulm alone some four million are annually exported, and about ninety thousand pounds are sold in the Paris markets every year.

The wild snails are collected and placed in small plots of land cleared of trees and covered with heaps of moss and pine-twigs, and separated from each other by moats, or trails of sawdust, for which snails have a natural antipathy. They are kept here and fed on fresh grass, cabbage leaves, mint, and other aromatic herbs. In the course of a week or ten days they have become quite obese and, besides, have attained a very delicate flavor; they are then starved for a few days to allow them to get rid of excrementitious matter, when they are ready for the market. To prepare them for the table they are well washed, then broiled, baked, or boiled, shell and all, when they are either extracted and served with various suitable sauces, or are placed on the table entire, to be removed at the time of eating by placing the shell to the mouth and drawing out the animal by sucking it.

The sea snails are not so extensively used as food, though in England the common periwinkle (*Littorina littorea*) is consumed in immense quantities by the poorer classes on the coasts as well as in London. About three thousand tons of them, valued at £15,000, are annually shipped to London alone.

There has been a number of cases of poisoning from eating snails which have been allowed to feed on hemlock and belladonna, so that now there has been an inspector appointed in Paris whose business it is to see that they are in fit condition for consumption.

In some persons the ingestion of snails brings on marked attacks of urticaria—the same as is seen in certain cases after eating clams, oysters, and other shell fish. In these cases it will be understood that there is a more or less marked idiosyncrasy in the person.

FIG. 5221.—Tachea Hortensis. (From Binney.)

An idea of the nutritive value of these mollusks may be gained from the following analysis of the "edible snail," made by Mr. Charles Mene:

Water	72.547
Nitrogeneous matter	17.652
Fatty substances	1.125
Non-nitrogeneous matter	6.300
Salts	2.176
Nitrogen	2.82%

In some parts of the world the snail has more or less of a reputation as a "cure" for consumption, concerning which it is only necessary to say that it may be considered a food of some value as affording a change of diet. *William Barnes.*

THYMUS GLAND, DEVELOPMENT OF.—The first statements regarding the development of the thymus gland contradicted each other completely. Arnold[1] asserted that it arose in common with the thyroid from the entoderm of the pharynx, while Bischoff[2] in general denied this. Remak,[3] in his great work, confirmed Arnold and added that this gland arises from one of the branchial clefts; but he was placed in doubt after Ecker had described the large gland in the neck of the chick as the thymus. From now on, the prevalent view continued to be that the thymus was mesodermal in origin.

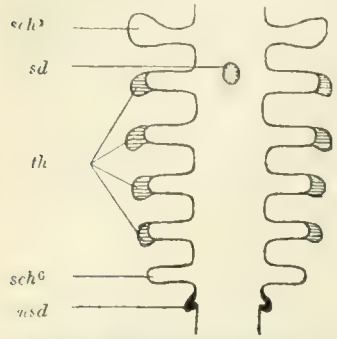


FIG. 5222.—Diagram showing the Branchial Clefts and the Glands arising from them in the Shark. (From Hertwig, after de Meuron.) *sch*¹, *sch*⁶, First and sixth branchial pockets; *sd*, thyroid; *th*, thymus; *nsd*, lateral thyroid.

We can well understand why these various views should be entertained when we consider that, for studies of this sort, the methods at that time were very crude; but in spite of all this we are under obligations to Remak for so much light regarding many problems in embryology, and it really seems a pity that his own view, which later on proved to be correct, should have been abandoned on account of his over-caution. By the more improved methods, both Kölliker[4] and His[5] observed that the thymus must be of epithelial origin, and therefore accepted the old view of Remak. It may be added that at this very same time two elaborate papers were published by Afanassiew[6] and Watney,[7] in which they attempted to demonstrate that the gland arises from the mesoderm. More accurate methods were now introduced, and it soon was demonstrated by Stieda[8] that in many animals the thymus arises from the third branchial pocket. This was also confirmed by Born[9] (and many others,[10, 19]), who in this study introduced his well-known method of reconstruction.

In the third part of his "Anatomie menschl. Embryonen," His[5] brought forth the view that the thymus arises from the sinus præcervicalis, and is therefore purely ectodermal in origin. This view he attempted to strengthen in a later publication,[20] and it was quite generally accepted. Later, however, in a response to a paper by the author,[14] His[21] retracts his older view and admits that the bulk of the thymus has its origin from the entodermal lining of the third branchial cleft. He therefore considers the origin of the thymus still an open question, and until more careful researches are made, accepts the view of Fischelis[22] and of Kastschenko,[23, 24] that is, that it arises from both ectoderm and entoderm.

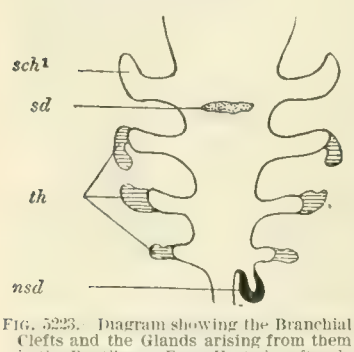


FIG. 5223. Diagram showing the Branchial Clefts and the Glands arising from them in the Reptiles. (From Hertwig, after de Meuron.) *sch*¹, First branchial pocket; *sd*, thyroid; *th*, thymus; *nsd*, lateral thyroid.

Shortly after the branchial arches are formed there appears at the dorsal side of each cleft a thickening of the entodermal cells, which soon separate from the entoderm to form distinct groups of glands. This is the condition of things in low vertebrates, and as the scale is ascended certain groups become more and more prominent, until man is reached, when only the two groups from the third branchial pocket remain to form the thymus.

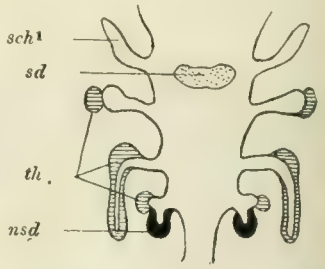


FIG. 5224.—Diagram showing the Branchial Pockets and the Glands arising from them in the Chick. (Modified from de Meuron.) *sd*, Thyroid; *sch*¹, first branchial pocket; *th*, thymus; *nsd*, lateral thyroid.

In the fishes the general relation of these glands to the branchial clefts is shown in Fig. 5222. These individual glands are soon united into one large gland on either side of the pharynx; in the bony fishes these groups unite into one gland before they have separated from the pharynx. In the reptiles the number of glands are reduced (Fig. 5223) to correspond with this number of branchial clefts. Van Bemmelen discovered in the elasmobranchs that the posterior cleft, or rudimentary cleft, produced a distinct body which did not unite with the thymus. This he has termed the suprapericardial body, and later its homology was found in many classes of vertebrates. In many reptiles it is unilateral, as shown in the figure. Considering their origin, they seem to be intimately related with the thymus, but in mammals it is probable that they are added to the thyroid, and will be discussed under that heading.

In birds the third branchial pocket gives the main origin of the thymus, as shown in Fig. 5224. Here we have a sharper line of demarcation between ectoderm and entoderm, as the branchial clefts do not break through as in fishes. We can now state with great certainty from what embryonic layer this gland arises, provided we have good serial sections to study. Very recently Kastschenko discovered a small gland in connection with the second branchial pocket, but as yet its fate has not been determined. It is no doubt a remnant of the portion of the thymus which arises from the same place in lower vertebrates. The third branchial pocket, however, becomes very prominent, grows toward the head, and is at no time blended with the ectoderm (Fig. 5225). To be sure, it comes in apposition with the ectodermal invaginations of the clefts, but recent work has shown that these have to do with the ganglia of the cranial nerves, and do not unite with the thymus as thought by His and others. Moreover, it is by no means probable that these sense organs of Froriep and Beard should suddenly leave the nerve ganglia in certain regions and unite with glands. Both observations and principles of development contradict this. The fourth branchial pocket, as well as a rudimentary fifth (fossa subbranchialis), gives rise to a few small bodies, the nature of which is not as yet truly known. That from the rudimentary fifth, no doubt, gives the gland which is homologous with Van Bemmelen's suprapericardial body.

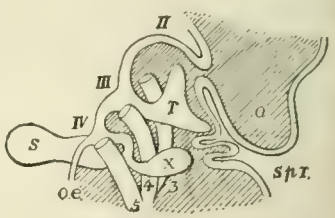


FIG. 5225.—Dorsal View of a Reconstruction of a Chick 110 hours old. × 35. *II*, *III*, and *IV*, Branchial pockets; *O*, operculum; *S*, thyroid; *spr*, sinus præcervicalis; *T*, thymus; *X*, body derived from the fourth branchial pocket; *oe*, œsophagus.

In mammals the condition of things is much simpler (Fig. 5226). The branchial grooves lie on the outside of the body, are shallow on their dorsal side, and deep on their ventral. As these arches fall over one another, the grooves as well as the third and fourth arches are buried in the side of the neck; while this is taking place a pit is first formed, the sinus præcervicalis of His.

From the dorsal side of the first groove an invagination unites with the ganglion of the fifth nerve; from the second, the invagination is to the ninth nerve; and from the third and fourth it is to the tenth nerve. A section through these organs in the region of the vagus and of the thymus is shown in Fig. 5227. The ectodermal invagination is absolutely blended with the vagus and is only in apposition with the thymus.

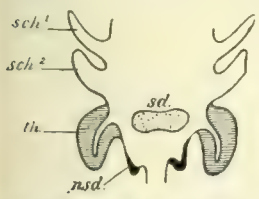


FIG. 5226.—Diagram showing Branchial Pockets, and the Glands arising from them in the Human Embryo. *sch*¹, *sch*², First and second branchial pockets; *th*, thymus; *sd*, thyroid; *nsd*, lateral thyroid.

The pharynx side of the branchial clefts presents about the same appearance as the external. The entodermal lining is in the form of slit-like pockets, which are better called branchial pockets, to differentiate them from the ectodermal side, or branchial grooves. As the head flexes upon the body the pharynx widens near the mouth and becomes narrower where the trachea is formed. There is a peculiar kinking of this region due to the rotation of the head. The first branchial pocket is converted directly into the Eustachian tube; the second disappears completely; the third forms the thymus (Fig. 5228); and the fourth becomes rudimentary and gives rise to the auxiliary thyroid glands.

The general appearance in the human embryo is quite similar to that in other mammals, as Fig. 5229 shows. Already in this early stage of development, the third branchial pocket shows an ingrowth which indicates the origin of the thymus. The portion of the cleft represented by the fundus (*F*) is not continuous with the thymus tube, and no doubt never plays any part in its formation.

The general view of the branchial pockets in a human embryo is shown in Fig. 5230. The whole pharynx is represented as a cast and the branchial pockets are represented by the figures 1, 2, 3, and 4. It is the one marked 3 which is destined to become the thymus. It soon becomes separated from the pharynx and then grows into the thorax.

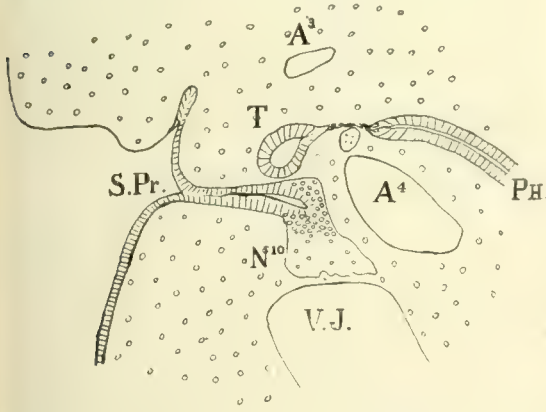


FIG. 5227.—Section through the Thymus and Fundus Præcervicalis of a Dog's Embryo, 10 mm. long. × 80. *Ph.*, Pharynx; *A*³, *A*⁴, aortic arches; *S.Pr.*, sinus præcervicalis; *V.J.*, jugular vein; *T.*, thymus still in connection with the pharynx.

Before the thymus is separated from the pharynx it contains a distinct lumen. This is soon lost in birds

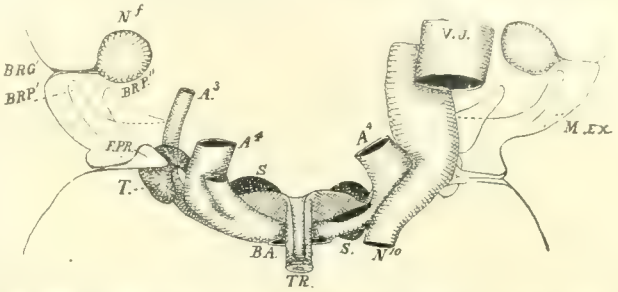


FIG. 5228. Dorsal Reconstruction of the Branchial Region of a Dog's Embryo, 10 mm. long. × 25. *Nf*, *N*¹⁰, Ganglia of facial and vagus nerves; *BRP'*, *BRP''*, branchial pockets; *BRG*, branchial grooves; *A*³, *A*⁴, aortic arches; *B A*, aortic bulb; *Tr.*, trachea; *M.ex.*, external meatus of the ear; *S*, thyroid; *T*, thymus; *F.PR.*, fundus præcervicalis.

where the thymus grows toward the head. In mammals, where the thymus grows into the thorax, the upper part contains a lumen, while the lower part grows by a mass of sprouts (Fig. 5231). This continues for quite a while until the whole organ is lobulated. New blood-vessels and lymph cells grow through the epithelial gland and change its nature. The entodermal cells become packed together into the Hassal's concentric bodies as shown by Maurer for the fishes, and by Ecker[25] and by His[26] for mammals. These bodies correspond with the "pearls" in carcinomata, which are present in cancers, that arise from the whole epidermis, as well as those from the œsophagus. The Hassal's bodies do not therefore indicate that the thymus arises from the ectoderm.

During the first two years of life the organ continues to grow and the two halves gradually approach each other more and more, until they seem as a single body. It now lies immediately in front of the heart, and often

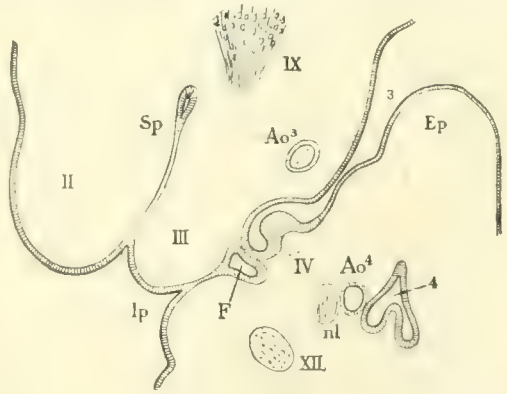


FIG. 5229.—Section through the Branchial Region of a Human Embryo, Five Weeks Old. (From Minot, after His.) *II*, *III*, *IV*, Branchial arches; *Sp*, second branchial grooves; *Ip*, infundibulum præcervicale; *F*, fundus of the infundibulum; 3, 4, third and fourth branchial pockets, with the thymus arising from the third; *Ao*³, *Ao*⁴, aortic arches; *Ep.*, epiglottis; *IX*, glosso-pharyngeal nerve ganglion; *XII*, hypoglossal nerve; *nl*, superior laryngeal nerve.

sends two horns which extend on either side of the neck to the thyroid, as is the case in the birds. From now on, the organ gradually atrophies.

In the study of the human embryo Sudler[27] finds no indication of the thymus in a human embryo of the second week, but in one of the fourth week the third visceral pouch appears as a ridge with a ventral free end, with no differentiation of tissue to suggest a thymus. In

an embryo four and one-half weeks old this ridge has disappeared and the third visceral pouch projects out

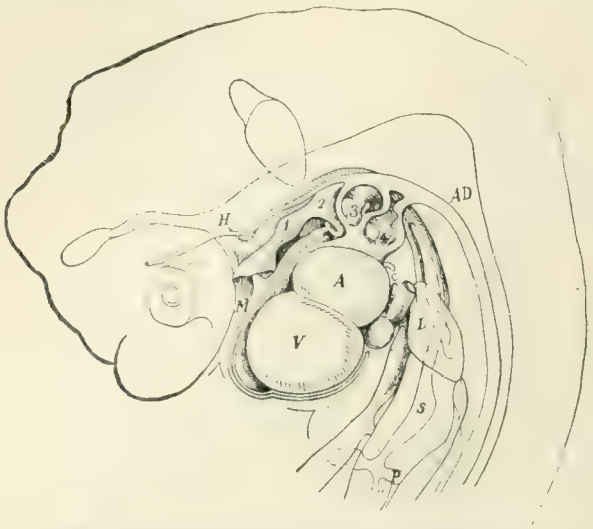


FIG. 5230.—Reconstruction of a Human Embryo Four Weeks old. (No. 2.) Enlarged sixteen times, and viewed from the left side. *H*, Hypophysis; 1, 2, 3, and 4, branchial pockets; *M*, mouth; *A*, auricle; *V*, ventricle; *AD*, descending aorta; *L*, lung; *S*, stomach; *P*, pancreas.

directly from the pharynx (Fig. 5232). In the next stage, of about five weeks, it is very similar to one described by Born, in which the thymus has become completely separated from the pharynx, and its original hollow is reduced to a crescent-shaped opening which is quite characteristic of the gland at this stage. The thymus now is a curved elongated body with an enlarged cephalic end. The lower end of this and the thyroid (Fig. 5233) run parallel, though without coming in contact with each other till the thyroid bends abruptly and crosses the middle line. An embryo slightly older shows practically the same conditions, the differences being that the enlarged head is relatively smaller and the general curve of the thymus is less. A small process projects dorsally and laterally.

FIG. 5231.—Thymus of a Rabbit Embryo Sixteen Days Old. (After von Kölliker.) *a*, Duct of the thymus; *b*, head of the thymus; *c*, posterior enlargement of the gland.

In an embryo of the sixth week the relative position of the thymus is lower and the division into different areas has disappeared. The head of the thymus is only slightly enlarged and the thymus and thyroid have both approached the middle line at the aboral end though still without meeting. In an embryo slightly older the thymus is still lower, so that the thyroid is higher even than the head of the thymus. The whole of the thymus projects beyond the thyroid and is nearer the middle line.

The oldest embryo studied was one of the seventh week, which shows the thyroid rudiment as having sunken relatively still lower. It is in contact with the thyroid along half of its upper surface, the lower end being free. In this free half the thymus and the thyroid approach each other and meet in the middle line where the ends are slightly swollen and bend ventrally. This appears to be a beginning of the folding of the thymus found in the adult organ. In this embryo the thymus shows the same

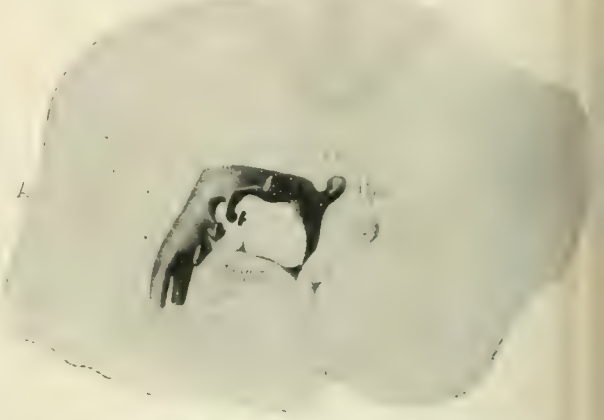


FIG. 5232.—Lateral View of a Human Embryo Four and One-half Weeks Old (No. 163). Enlarged ten times. (After Sudler.) *Hyp.*, Hypophysis; *Oe*, œsophagus; *Thyr.m.*, median thyroid rudiment; *Tr*, trachea; *V.Pi–V.Piv*, first to fourth visceral pouches.

lack of bilateral symmetry which is apparent in the development of the pharynx in the human embryo as

FIG. 5233.—Lateral View of the Pharynx of a Human Embryo Five Weeks Old (No. 109). Enlarged ten times. (After Sudler.) *N*, Nose; *L*, larynx; *Tr*, trachea; *Thym*, thymus; *Thyr.m.*, median thyroid; *V.Pi–VPiv*, first to fourth visceral pouches.

well as that of some other animals. In this the rudiment extends a little higher on the right side than on the left.

From the study of these embryos it is apparent that in man the rudiment of the thymus arises from the entoderm of the third visceral pouch. *Franklin P. Mall.*

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THYROID GLAND, DEVELOPMENT OF.—Shortly after Rathke discovered the branchial arches in higher animals, Huschke[1] advanced the idea that the thyroid gland arises from the first arch. Later, however, he states that after the arches disappear the thyroid remains as their remnant. A year later, Rathke[3] asserted that the thyroid arises as a bilateral organ from the posterior part of the trachea, immediately behind the larynx. This view was affirmed by Arnold.[4] Bischoff[5] accepted neither of these views, but added a third. According to him, the thyroid arises as a bilateral organ from the blood-vessels on either side of the neck.

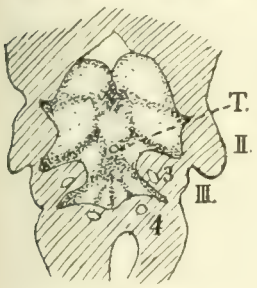

FIG. 5234. Reconstruction of the Mouth of a Chick Eighty-eight Hours Old. The floor of the mouth is exposed by cutting off the back of the head. Dorsal view. × 20. *T.*, Tuberculum impar, back of which is the opening of the thyroid; *II*, *III*, branchial arches; 3, 4, third and fourth aortic arches.

The first careful investigations were made by Remak[7] upon the chick. In this subject, as well as in many others in embryology, he was the first to give accurate information. He found that the thyroid is entodermal in origin and arises from the ventral median line of the pharynx. At first it appears as a single vesicle, which soon divides into two parts, each half lying on either side of the trachea. Götte,[7] Müller,[8] and Seessel[9] confirmed Remak's views in general, differing only in minor points. They discussed whether or not the organ divided is a vesicle or is a solid body, although none of them found stages in which the thyroid was dividing. Remak placed the origin of the thyroid at seventy-nine hours in the chick; Müller in the third day; and Seessel very definitely in the second day before the head flexed upon the body.

His[10] revived the old view of Rathke by discovering that certain bodies arise from either side of the pharynx; he believed them to be the thyroid and the auxiliary thyroid of Remak. According to the illustrations which accompany his paper, the gland arises from the branchial cleft between the second and third aortic arches, therefore the second cleft. Later, however, he abandoned this view and accepted that of Seessel, who worked under his guidance. Later, Kölliker[11] accepted the old Remak-Seessel view for the rabbit, as His[12] did for man.

This group of excellent workers seemed to set the subject aside for a while, but, immediately following their work, two authors simultaneously described the thyroid as being bilateral in origin, arising from a branchial cleft on either side of the neck. Stieda[13] proved definitely that a glandular organ arises from the clefts on either side of the neck, but did not know from which cleft, although he was inclined to accept the fourth. Wölfler[14]

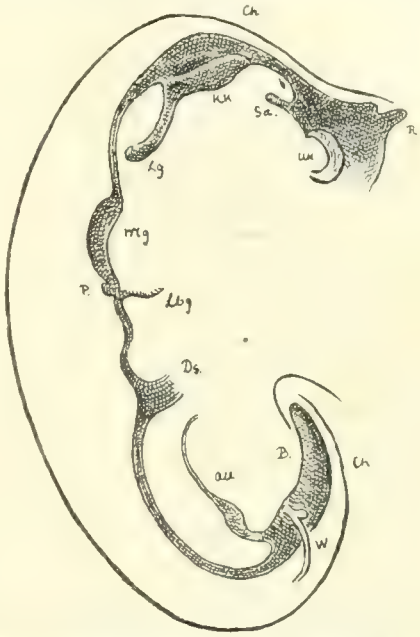

FIG. 5235.—Alimentary Canal of a Human Embryo. × 20. (After His.) *Uk*, Lower jaw; *Sd.*, thyroid; *Lg.*, lung; *Mg.*, stomach; *P.*, pancreas; *Lbg.*, bile duct; *W.*, Wolffian duct.

did not employ very accurate methods, and therefore got the location of the origin of the gland in the first branchial cleft—the one which later forms the Eustachian tube. He was so enthusiastic over his discovery that he denied altogether a median thyroid, although he had never seen the thyroid in connection with any cleft. Discussions naturally bring forth more accurate investigations, and in this case they bore their fruits in Born's paper.[15] The paper of Born not only threw a great deal of light upon the subject in question, but also added

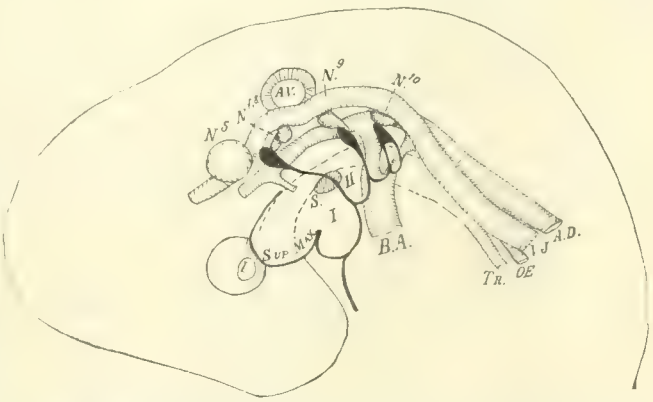

FIG. 5236.—Profile Reconstruction of a Dog's Embryo, 6 mm. long. × 25. *N⁵*, *N⁸*, *N⁹*, *N¹⁰*, ganglia or cranial nerves; *I*, *II*, branchial arches; *AV.*, auditory vesicle; *Tr.*, trachea; *OE.*, œsophagus; *V.J.*, jugular vein; *A.D.*, descending aorta; *B.A.*, bulbus aortæ; *S.*, thyroid gland.

greatly to our methods of investigation. He introduced a method which to us now seems so logical that it is a surprise that it was not employed earlier. He began with embryos of the pig before the thyroid appeared, and

followed them stage by stage until the organ was fully formed. In each stage the enlarged sections were drawn upon wax plates of the proper thickness, then cut out and the pieces piled upon one another, thus forming very accurate models of the various specimens studied. He then followed the lateral thyroids of Stieda and Wölfler, and found that later on they were added to the median thyroid of Remak. The great difficulty was therefore solved by this method. Instead of these various authors contradicting one another, they in reality described correctly only different portions of the same story. According to Born the lateral thyroids arise from the fourth branchial clefts. Since then, Born's view has been confirmed in a variety of mammalian embryos by different writers.[16–25]

The subject of the origin of the thyroid and thymus (see *Thymus*) has been greatly complicated by a group of glands which arise from the degenerating branchial clefts and form the so-called auxiliary thyroid glands. From a phylogenetic standpoint all glands which arise from the clefts must be viewed as thymus. The great bulk of thyroid arises from the ventral wall of the pharynx in the region of the second cleft. As the clefts gradually disappear in the evolution of the vertebrates, the glands from the hindermost clefts no longer unite with the main bulk of the thymus, and often remain as distinct glands —the suprapericardial bodies of van Bemmelen, accessory thyroids of de Meuron, post-branchial body of Maurer, or as the corpus Y of the writer.[26] In the mammals the main bulk of the thymus arises from the third cleft, and the auxiliary thyroids seem to unite with the median thyroid as described by Born. In spite of the great amount of work which has been done upon this subject, it still seems to the writer that there is yet considerable darkness regarding it.

The general view is that the thyroid has three distinct origins in nearly all vertebrates —a median and two lateral. The median arises from the ectoderm of the middle line in the neighborhood of the second branchial arch (Fig. 5234), and the lateral from the most posterior branchial clefts; in mammals, the fourth.

The median thyroid arises in all vertebrates from the entoderm of the pharynx shortly after the branchial arches are well formed (Fig. 5235). This has been known since the time of W. Müller, and, although contradicted many a time, has of late been verified by so many careful observers that there is no longer any doubt whatever regarding it. In some mammals (the dog, for instance) it arises as a vesicle, which becomes solid before it separates from the pharynx, and when separated soon becomes lobulated. It now gradually shifts itself into the tissue of the neck, and in early stages lies in front of the aorta just as it leaves the heart (Fig. 5236). The median gland now becomes constricted into two parts, one of which is situated on either side of the neck, but they remain connected by a band—the isthmus. Its origin in the human embryo is much the same (Figs. 5237 and 5238). According to His, it remains a vesicle for quite a long time, and the separation from the pharynx occurs quite late or may not take place at all. Later, however, the formation of the ligamentum hypothyroideum cuts the duct (*d. thyreoglossus*) into two, thus forming two ducts. The half communicating with the mouth has been termed by His *ductus lingualis*, and the one with

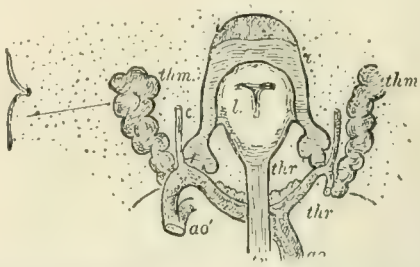

FIG. 5238.—Reconstruction of the Thyroid, Thymus, and Pharynx of a Human Embryo Five Weeks Old. (Slightly modified from His.) *thm*, Thymus; *thr*, thyroid; *c*, carotid; *ao'*, ascending aorta; *ao*, descending aorta; *tr.*, trachea.

the thyroid as the *ductus thyroideus*. His has found the ductus lingualis in five adults, and in all cases the ductus thyroideus was present also. The latter is always embedded in a median lobe of the thyroid, and the former opens into the foramen cæcum of the tongue. The ductus thyreoglossus may be broken into a series of vesicles, as first described by Verneuil, but as a rule it disappears fully, its only remnant being the foramen cæcum.*

The lateral thyroids were first demonstrated by Stieda and by Born, although Rathke, His, and others had in all

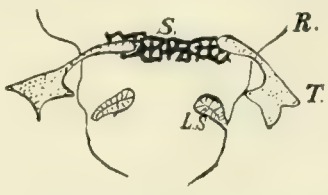

FIG. 5239.

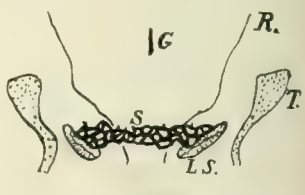

FIG. 5240.

FIGS. 5239 AND 5240.—Diagrams of Two Stages of the Development of the Lateral Thyroids. (Slightly modified from Born.) *R*, Border of the pharynx; *T.*, thymus; *G*, glottis; *L.S.*, lateral thyroids.

probability described them from time to time. The true meaning of them was fully made out by Born and by de Meuron, the former having discovered that they unite with the median thyroid in mammals, the latter having studied them from a comparative standpoint. Diagrams of the branchial pockets for some of the different classes of vertebrates are given in the article *Thymus*, and by them it is shown that a rudimentary branchial pocket exists in all of the classes. In certain reptiles there is but a single one on the left side, the one on the right not having developed. We can view this state of things only as an intermediate one between the reptiles (in which they develop on both sides) and the birds. In all classes the hindermost cleft gives rise to a distinct gland known as the suprapericardial body of van Bemmelen and as the accessory thyroid of de Meuron.[28–30] In the selacians these bodies remain far away from the median thyroid, and they never unite with it. In higher animals they gradually approach the median thyroid nearer and nearer, and in mammals they unite completely with it. Fig. 5238 shows the general relation of these glands in a human embryo before the lateral thyroid is fully separated from the pharynx. Figs. 5239 and 5240 show two stages in which the lateral thyroid is approaching and uniting with the median. This is brought about by a

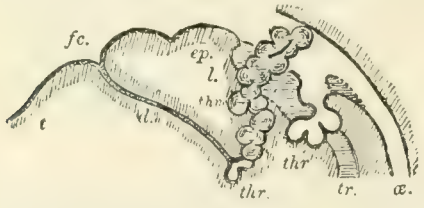

FIG. 5237.—Pharynx, Thyroid, and Thymus of a Human Embryo, × 25. (From Quain, after His.) *tr.*, Tongue; *fc.*, foramen cæcum; *ep.*, epiglottis; *thm.*, thymus; *thr.*, median thyroid; *thr'*, lateral thyroid; *d*, ductus thyreoglossus.

* From the standpoint of evolution it is interesting to note that Dohrn[27] has advanced the hypothesis that the thyroid represents a lost branchial cleft. These speculations are, of course, the natural outcome when genetic relation is taken into consideration in the study of comparative embryology.

double shifting. The median thyroid sinks deeper and deeper into the tissue of the neck, and practically lies in contact with the lateral thyroids before they separate from the pharynx. When these in turn separate from the pharynx they are shoved into the tissue of the median thyroid instead of into the ordinary mesoderm tissue of the neck.

It will be noticed that the lateral thyroids do not always arise from the same branchial clefts: in selacians from the seventh; in reptiles from the fifth; in mammals from the fourth. It is only in mammals that they really unite with the median thyroid. Viewing the thing from the standpoint of homology, what is lateral thyroid in mammals is thymus in lower animals; in both selacians and reptiles the fourth cleft gives rise to a portion of the thymus. We must therefore view the lateral thyroid as a portion of the thymus which is now united with the thyroid. In lower animals the secondary union of the gland from degenerating clefts with the median thyroid does not take place, and they remain in the tissue of the neck, as in the auxiliary thyroid glands, which have perplexed so many investigators. According to Kastschenko the lateral thyroid of mammals plays a very minor part in the formation of the mature organ, while according to His it forms the major part. A true blending of the two does, however, take place, as shown by the investigations of Born and of His (Fig. 5241).

The further development of the thyroid is by means of sprouting, so that the enlarged organ is a plexiform mass of cylinders of epithelial cells. Blood-vessels grow in between them, and soon the cylinders show constrictions which cut them up again and again. They now become hollow, and at the same time there is a secretion of the colloid substance. The cut-up cylinders become more and more distended, and thus the adult thyroid is composed of a mass of hollow spheres covered with a layer of epithelial cells and filled with colloid substance. When half of the thyroid is removed by an operation or otherwise, the remaining portion soon loses its colloid and returns to its "embryonic state." It enlarges to its former size and again forms the colloid spheres much after the fashion it did in the embryo.[31]

In the human embryo Sudler[32] finds the thyroid rudiment in the earliest one studied, an embryo at the end of the second week. It appears as a rounded eminence on the ridges uniting the first pair of visceral pouches. Its outline is elliptical, being broader from side to side than it is ventrodorsally. This is the rudiment of both the thyroid gland and the ductus thyreoglossus.

In an embryo of the fourth week the rudiment appears as a solid body extending dorsally from the apex of the

FIG. 5241.—Section through the Thyroid of the Embryo of the Pig, 21.5 mm. long. × 80. (From Hertwig, after Born.) *tr.* Trachea; *LS.*, lateral thyroid; *MS.* median thyroid; *g. g.* blood-vessels.

angle formed by the meeting of the first visceral pouches (Fig. 5242). Just oral to it is the hollow cavity representing the inner of the second visceral arches and directly aboral is the hollow cavity representing the tuberculum impar. Its appearance is that of a knob on a short slender stem. The fourth visceral pouch at this stage shows no thickening or development into the lateral thyroid rudiment.

In an embryo of four and one-half weeks the thyreoglossal duct remains as a small conical eminence on the

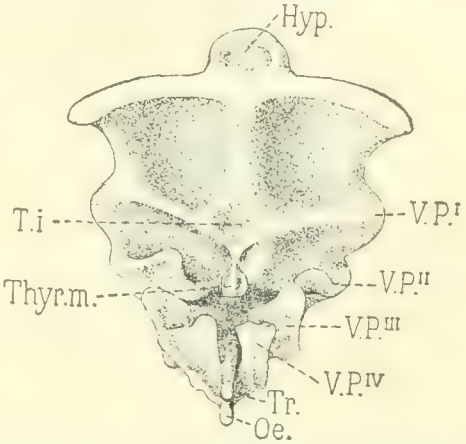

FIG. 5242.—Ventral View of a Model of the Pharynx of an Embryo Four Weeks Old (No. 2). (After Sudler.) *Hyp.*, Hypophysis; *Oe.*, œsophagus; *T.i.*, depression of the tuberculum impar; *Thyr.m.*, median thyroid rudiment; *Tr.*, trachea; *V.P.*I–*V.P.*IV, first to fourth visceral pouches.

ridge connecting the first visceral pouches. It is at the junction of the tuberculum impar and the two dorsal rudiments of the tongue (Fig. 5243). The median thyroid rudiment has become entirely disconnected and has sunk to the level of the third visceral fold. It has spread out laterally and has a bilobed structure. The left lobe

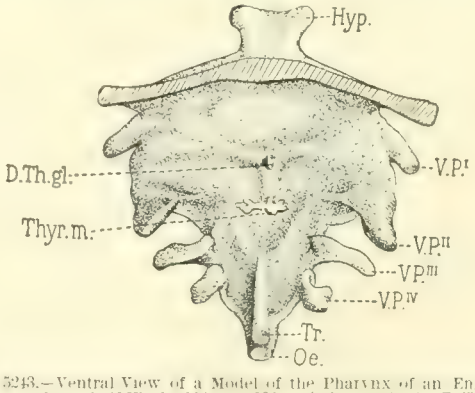

FIG. 5243.—Ventral View of a Model of the Pharynx of an Embryo Four and One-half Weeks Old (No. 163). (After Sudler.) *D.Th.gl.*, ductus thyreoglossus.

is much the longer and approaches closer to the floor of the mouth than the right. In this the fourth visceral pouches appear as two ventral projections with enlarged knobs bent sharply dorsal.

In an embryo of five weeks the median thyroid rudiment has become **U**-shaped, though the left arm is much longer than the right (Fig. 5244). Its outline is quite irregular. In this the transverse part of the **U** which runs across the middle line has sunk to the level of the fourth visceral pouch. This part shows the usual network structure formed by cords of solid cells. The arms are crescentic in cross section, with the hollow looking away from the middle line and embracing the thymus, although the two do not come in contact. The lateral thyroid rudiments, which consist of hollow tubes surmounted by solid expansions, are still connected with the

pharynx. The two sides are unsymmetrical. On the right side the ventral knob is smaller than the dorsal, while on the left they are about equal in size and placed on the same level.

In an embryo only slightly older the median thyroid is still **U**-shaped, though the right arm is still smaller than

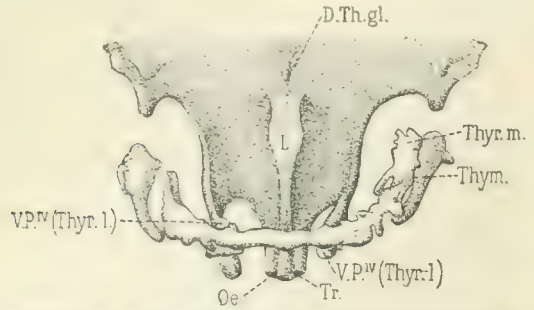

FIG. 5244. Ventral View of the Pharynx of an Embryo Five Weeks Old (No. 149). (After Sudler.)

in the last and not so long as the one on the left side. The lateral rudiments show in this embryo the greatest lack of symmetry of any of those studied by Sudler (Fig. 5245). The right rudiment is still connected with the pharynx by a small hollow stalk, while on the left side this connection has entirely disappeared. On the right side the ventral knob touches the middle of the right arm of the median rudiment, but there is no histological continuity, whereas on the left side the ventral knob not only touches the median rudiment, but there is actual continuity. As in the embryo described before, the ventral knob on the right side is much smaller than the dorsal one, while on the left side they are of almost the same size.

The median and lateral thyroid rudiments have united on both sides in an embryo of the sixth week, and all connection with the pharynx has disappeared. They still appear as distinct rudiments.

In a slightly older stage the lateral rudiments and the median have so completely united that all there is to show that they were once separate are a few prominent lobules at their point of union. The loop of the **U** has become smaller and the arms larger, and they have become lobulated, so approaching the condition of the adult gland.

In the last embryo studied, one of the seventh week, the shape is almost that of the adult thyroid. The two lateral lobes are pyriform and are connected by a small isthmus, which is attached to them at the smaller end.

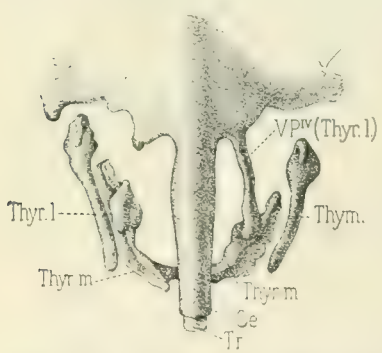

FIG. 5245.—Dorsal View of the Pharynx of an Embryo 13 mm. long (No. 175). (After Sudler.) The lateral thyroid on one side is attached to the pharynx and on the other is separated from it.

In the human embryo, as well as in the bird and some of the mammals, the pharynx develops more slowly on the right side than on the left, and the most striking example of this is in the thyroid. This may be due to the development of the heart and the bending of the head to the left.

From these different embryos Sudler draws the conclusion that "the thyroid arises in the human embryo from the union of a median rudiment situated at the point of junction of the tuberculum impar and the two dorsal rudiments of the tongue with a paired rudiment arising as a differentiation of a lining of the fourth visceral pouch." *Franklin P. Mall.*

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TICK FEVER, OR SPOTTED FEVER.—A disease known by the latter of these two names is found in the States of Montana, Idaho, Nevada, Wyoming, and Oregon. As two other diseases (viz., typhus fever and cerebro-spinal meningitis) are already known as spotted fever, it would be well, as suggested by Anderson, to call the disease under discussion tick fever.

ETIOLOGY.—Tick fever or spotted fever is found in the mountainous districts in the above-named States at an elevation of over three thousand feet. It does not seem to be prevalent outside the latitude of 40° to 47° N. The disease is only found in persons whose occupation causes them to be exposed to the bite of the tick; such are lumbermen, ranchmen, and sheep-herders. Males in the prime of life are most liable to the disease; this would be expected from the occupations just mentioned. Beyond this, age and sex have no etiological significance. The disease is in all probability caused by a parasite.

The Parasite.—"Wilson and Chowning noticed ovoid intracorpuscular bodies in stained preparations of the blood from their earlier cases. They did not determine the character or significance of these bodies until they examined the fresh blood, when they found ovoid intracorpuscular bodies showing amœboid movements. These observations they confirmed in all the later cases which they examined. To Wilson and Chowning, then, belongs the credit of discovering a parasite which is very *probably* the cause of spotted (tick) fever." Anderson further says that in his studies upon the cause of this disease he "had the opportunity of examining the blood, both fresh and stained, in a number of cases. Two cases were in a hospital in Missoula, and daily examinations were made. In the fresh blood a few cells were found to contain parasites. Three forms were seen. The most common was a single ovoid body, refractile, situated within the cell, usually near its edge. When the slide is warmed this body possesses the power of projecting quite rapidly pseudopodia and of effecting a slight change of position. This form, which is apparently an early or young form, is about 1.5–2 μ in length, and 0.5–1 μ in width at its widest part. It closely resembles the earliest intracorpuscular parasites of æstivo-autumnal malaria.

"Another form, not so common, was larger, being about 2–2.5 by 1–1.5 μ, larger at one end and showing in the larger end a dark granular spot; this was also amœboid.

"The third form noted was arranged in pairs, distinctly pyriform, with the smaller ends approaching, and in two cases a fine thread uniting the small ends was seen. Motion was not observed in this form, but the spot mentioned in the second form was seen.

"The parasites are never found in very large numbers, it being usually necessary to search several fields of the slide to find one. Sometimes they occur in groups, two or three infected cells being found in one field. In both fresh and stained preparations extracorpuscular bodies closely resembling the small single intracorpuscular form were seen. I was unable definitely to decide the character of these bodies, but am strongly inclined to think that they are the young form of the parasite which has not yet invaded the red cells.

"In the cases of spotted (tick) fever which I had the opportunity of examining I had no great difficulty in finding both in fresh and in stained preparations the bodies above described. Their constancy in the blood of persons suffering with spotted fever, their persistence for some time in the blood of these persons after recovery, their absence from the blood of persons suffering from other diseases and of healthy persons make it very probable that they are the cause of the disease, and that one more has been added to the rapidly growing list of diseases of man due to animal parasites." (Anderson: "Spotted Fever (Tick Fever) of the Rocky Mountains.")

Method of Infection.—"The life history of the organisms of malaria and Texas fever naturally suggested that some insect was concerned in the transmission of the disease. On investigation it was found that the ticks appeared in the valley about the last of February, but were inactive until the middle of March or 1st of April, the first cases of fever appearing about the last of March. The ticks begin to diminish greatly in number from about June 1st, and after the middle of July very few are seen; the cases of fever also begin to diminish about June 1st, the latest date on which the disease has been known to occur being July 20th.

"Mosquitoes do not appear in the valley until after the first cases of fever develop, and remain some time after the last cases appear. Bedbugs and other house insects, I think, were well excluded, by the fact that there has never been known an instance in which two cases occurred the same year in the same house.

"On a closer study of the cases of spotted (tick) fever it was always found that there was a history of tick bites about one week before the onset. In four cases there was a history of a single bite two, three, five, and seven days, respectively, before the initial symptoms. The usual time between the bite and the onset of the fever is about seven days. If the tick transmits the disease, it may be asked, Why do not more persons become infected, and why is the infection confined to the west bank of the Bitter Root River? I think this may be answered by the very obvious fact that the tick is unable to travel any great distance, unless carried on some person or object. Again, it is very unusual for a tick to bite a person and not be discovered in a short while, and the result is the death of the tick. If, as in Texas fever, the development of the parasite takes place in the female tick and the young ticks transmit the infection, the very small number of ticks which escape detection in persons explains the small number of infected ticks. Where do the female ticks get their infection? I examined a recovered case twenty-four days after discharge by the physician and had no trouble in finding the parasite in the fresh blood. This child had been out of doors for over two weeks, and if a female tick (ticks were quite numerous near the house) had bitten her and escaped destruction the parasites in the blood taken in by the tick would have undergone development, and the young ticks, when hatched out, would be ready to infect prospective victims.

"While the above facts and conclusions tend strongly to the belief that the ticks are necessary for the transmission of the disease, the actual fact cannot be proved scientifically until carefully controlled experiments are made on non-immune persons." (Anderson, *ut supra.*)

The tick in question is in all probability *Dermacentor reticulatus.*

Morbid Anatomy.—Rigor mortis is intense, and appears early. The skin is jaundiced, has a mottled appearance, and the wounds caused by the tick bites may be present. Petechial spots, bright to dark purple in color, and from 1 to 3 cm. in diameter, are found, chiefly on the wrist, ankle, arm, and leg. The spleen, liver, and pancreas are much enlarged; the kidneys are also enlarged.

Symptoms.—There is a period of incubation of about a week. The patient complains of nausea, general malaise, and a chill; this latter is followed by a fever which reaches its highest point about the tenth day, is characterized by evening rise and morning remissions, lasts about two weeks, and may be followed by subnormal temperature. In severe cases the morning remissions may be absent, and the fever remains high (from 104° to 106° F.). There are general pain and soreness, particularly during the first week, coated tongue with red edges, sordes, constipation, nausea which persists in severe cases, scanty urine with albumin and casts, and epistaxis. The liver and spleen may be enlarged. The pulse is high, and out of all proportion to the fever; the respiration is also increased. An examination of the blood shows: (1) the parasite described above; (2) a decrease in the percentage of hæmoglobin; (3) a decrease in the number of the red blood cells; (4) a slight leucocytosis, chiefly of the large mononuclears. Bronchitis is present during the second week; and in severe cases lobar pneumonia supervenes, with a grave prognosis.

"*The eruption* appears usually on the third day, first on the wrists and ankles, then on arms, legs, forehead, back, chest, and, last and least, on the abdomen. It is never very abundant on the abdomen, but the other portions of the body, in some cases, are literally covered by the eruption.

"At first the spots are of a bright red color, macular at all times, from a pin point to a split pea in size. At first they disappear readily on pressure and return quickly, but if the case is a severe one they soon become darker and in some cases are almost purple. From about the sixth to the tenth day of the disease they fail to disappear on pressure and are distinctly petechial in character. In favorable cases, about the fourteenth day, they begin to lose their petechial character and disappear slowly on pressure. In some cases the eruption consists of small, brownish spots, giving a turkey-egg appearance.

"As the fever declines the eruption begins to fade; but a slight return of fever or a free perspiration will cause it to show distinctly.

"When convalescence is well advanced desquamation begins and extends over the entire body. In very severe cases there may be gangrene of the fingers or toes, and still more frequently of the skin of the scrotum and penis. The skin is always jaundiced to a greater or less degree. This is usually first noticed in the conjunctivæ, the vessels of which are congested from the outset." (Anderson, *ut supra.*)

	Tick fever or spotted fever.	Typhoid fever.	Typhus fever.
Contagion	Non-contagious.	Not contagious in the ordinary acceptation of the term.	Very contagious.
Geographical distribution.	From 40° to 47° N.	Universal	Almost universal.
Season	March to July	All the year; chiefly July to November.	Generally in the winter.
Eruption—			
Date of occurrence.	Third day	Second week	Third to fifth day.
Site of first appearance.	Wrists and ankles, arms and legs.	Abdomen and back.	Abdomen, flexor surfaces of forearms, and general, except on face.
Blood examination.	Shows parasite.	Eberth's bacillus in cultures from blood. Widal reaction.	Negative.

Diagnosis.—This is made from: (1) The case occurring in the region known to be infected; (2) history of a tick bite; (3) the eruption appearing on the third day, and being seen first on the wrist and ankles; and (4) the presence of the parasite in the blood. The diseases from which it is to be differentiated are typhoid fever and typhus fever, particularly the latter. The preceding table will assist in making a diagnosis.

Prognosis.—This is unfavorable. Up to the present the death rate from tick fever has been seventy to ninety per cent. in Montana; but in Idaho and Nevada it is much lower. The disease varies in malignancy both in different localities and in different years in the same locality.

Treatment.—The treatment has so far been unsatisfactory; but in five cases, all treated by quinine, all recovered. Anderson suggests the bimuriate of quinine, 1 gm. (gr. xvi.) hypodermatically, q. 6. h.; or, by mouth, the sulphate of quinine in similar doses, q. 4. h. This drug should be given persistently from the commencement of the disease. The treatment is otherwise symptomatic, and includes cardiac stimulants, Dover's powder for the pains and soreness, tepid baths for the fever, and plenty of water to flush out the kidneys. The site of the tick bite should be cauterized with ninety-five-per-cent. carbolic acid. *R. J. E. Scott.*

Reference.

Anderson, John F.: Spotted Fever (Tick Fever) of the Rocky Mountains. Bull. No. 14, Hyg. Lab., U. S. Pub. Health and Marine-Hospital Service, Washington, p. 50. From this pamphlet, which gives all that is known of spotted, or tick fever, the above article has been compiled.

TYPHOID FEVER, BACTERIOLOGY OF.—The bacillus of typhoid fever was discovered by Eberth in 1880, but not until four years later was it obtained in pure culture. This pure culture was isolated by Gaffky from the spleen and mesenteric lymph glands of patients dying from typhoid fever. In cover-slip preparations from pure cultures it stains well with any of the ordinary aniline dyes.

Morphology.—The morphological characteristics of this organism are as follows: Its length varies from 1 to 4 μ, its diameter from 0.4 to 0.9 μ. The ends are always rounded. In cultures, and more especially in potato and old bouillon cultures, these organisms are often found grouped together in chains, sometimes as many as four or five in a chain. They are rapidly motile, this motility being due to the fact that they possess flagella, the number of which varies from eight to twenty. These flagella are attached to the bacillus at all points of its surface, that is, not only on the ends, as is the case in many bacteria, but also at its sides. For demonstrating these it is necessary to use a special method of staining. In my experience Loeffler's method has proved to be the best. Take two cover slips which have been thoroughly cleansed and are free from grease, and place on each one of these a drop of sterile water; then with a platinum needle touch the surface of an eighteen-hour agar culture of the bacillus, and draw the needle thus charged through first one drop and then the other; finally, cause the drop to spread out over a larger area and allow it to dry. By this method we obtain a good dilution in parts of the smears. There is no need to fix in the flame, as the mordant is a good fixative. The solutions required are as follows: First, a twenty-per-cent. aqueous solution of tannic acid; second, a saturated aqueous solution of ferrous sulphate (not to be heated); third, a saturated alcoholic solution of either fuchsin or gentian violet. Take of solution number one, ten parts; of number two, five parts; and of number three, one part. Let them stand for an hour and then filter; use at once. Flood the cover slip with this mordant (either of the first two solutions) for one minute, and then wash gently in distilled water; drain off the excess of water, and flood the slip with aniline fuchsin or aniline gentian violet, and warm carefully for one minute. Do not heat sufficiently to produce steam. Wash again in water and dry; then mount in Canada balsam. Another good method is that described by L. Smith in the *Journal of Medical Research*, vol. i., new series, p. 341. The dye which he uses is night blue; it gives a very beautiful picture, and is very easy to manage.

Cultural Characteristics.—The bacillus grows best at body temperature (37.5° C.), but it grows well at room temperature. Its thermal death point is 60° C., after an exposure for twenty minutes. According to Park the organism will live for five months when frozen, but not longer. It grows well on all media. In bouillon it forms a uniform cloud throughout the tube, and often will develop a heavy pellicle on the surface. On agar it produces a growth of a pearly white; on gelatin the growth is whitish and no liquefaction takes place; on potato the growth can hardly be seen at the end of forty-eight hours, but still older cultures may show a dirty-yellow growth. This organism grows well in milk without the production of acid from the lactose. There is, however, a slight primary production of acid. It does not coagulate the milk. In Dunham's solution it does not form indol. It does not cause any of the sugars to ferment with gas production. These last three cultural characteristics are used as a means of differentiating the typhoid bacillus from the colon and paracolon and the paratyphoid groups.

During the past few years there have been isolated from patients suffering from what seemed clinically to be a typhoid infection bacilli which did not answer culturally to the Bacillus typhosus, and did not agglutinate in serum which agglutinated this bacillus. The serum from the patient from which the organism had been isolated did not agglutinate the typhoid bacillus, but did agglutinate the isolated organism. These organisms when tested culturally behaved in some ways like the B. typhosus, while in other ways their behavior was like that of the Bacillus coli communis; hence they have been termed intermediates, and some bacteriologists have gone so far as to divide them into sub-groups. The organisms are often spoken of indiscriminately as para-typhoid or paracolon bacilli.

So many of these intermediates have been isolated that it will be impossible to discuss them all here. It might be stated, however, that the great majority of the cases suffering from infection with these intermediate organisms have run a very mild course, and they do not seem to be as pathogenic a group, on the whole, as that of the Bacillus typhosus.

The following short table will give a good idea of the position of this group:

	Bacillus typhosus.	Intermediates.	Colon bacillus.
1. Formation of indol in Dunham's solution in forty-eight hours.	Negative results.	Some positive results.	Positive results.
2. Coagulation of milk	Negative results.	Negative results.	Positive results.
3. Fermentation with production of gas in			
(*a*) glucose bouillon	Negative results.	Positive results.	Positive results.
(*b*) lactose bouillon	Negative results.	No positive results.	Positive results.
(*c*) mannit bouillon	Negative results.	Some positive results.	Positive results.
4. Agglutination with specific serum—			
(*a*) typhoid serum	Positive results.	Negative results.	Negative results.
(*b*) intermediate serum	Negative results.	Positive results.	Negative results.
(*c*) colon serum.	Negative results.	Negative result.	Positive results.

Of the intermediates which have thus far been isolated, the following are among the more important, historically as well as bacteriologically: Gaertner's, Cushing's, Gwyn's, Schottmüller's, Buxton's, and Libman's.

Agglutination.—This phenomenon does not belong exclusively to the subject of this article, but I shall treat

of it fully for two reasons: first, because it was the study of this reaction with the B. typhosus that stimulated a great amount of research in regard to this phenomenon as an aid to diagnosis; secondly, because of the importance of this test and on account of the many errors to which it may lead unless it be fully understood. In 1884 Charrin and Roger, while working with the Bacillus pyocyaneus, observed the clumping of the bacilli, but they pushed their study of this phenomenon no further, and it was not till 1896 that it was again brought forward, this time by Gruber and Durham. These investigators immunized animals against various strains of bacteria, and they found that the serum of these animals had the property of clumping the bacteria when the bacteria were brought in contact with it; and, furthermore, they found that this action was fairly specific, that is, the serum from any animal which they had immunized would only clump the species of bacteria which had been used to bring about this immunization. They therefore advocated that this phenomenon be utilized for the purpose of differentiating species of bacteria. They did not, however, in their published work, suggest the use of serum taken from these patients as a means of determining what species of bacteria were causing the infection.

During this same year (1896) there was published a paper by Widal and Grünbaum in which they outlined a clinical test for typhoid fever based on the phenomenon of clumping. They were the first, therefore, to point out the value as a means of diagnosis, and the first also to devise a technique for carrying out the test. Since their paper was published this test has been used in all parts of the world, and legion are the papers that have been published on it.

The Technique.—The requisites are: 1. An actively motile culture of B. typhosus. This is best obtained by emulsifying a twenty-four hours' old agar culture in 10 c.c. of an 0.85 per cent. sodium-chloride solution; or by transferring from three to six loopfuls of a twenty-four-hour agar culture to a tube containing bouillon, shaking this thoroughly and incubating at 37° C. for an hour or two; or else one may transplant the typhoid bacilli from day to day into tubes of bouillon and let the growth proceed on the top of the thermostat. 2. The blood to be tested may either be in a dried condition or else it may be collected in capillary tubes and the serum obtained from these after coagulation. By the latter method we can measure our dilutions with almost perfect accuracy, a thing which it is impossible to do if we use a dried specimen. In the latter case it is necessary to dissolve out the substance representing the serum by letting the water used for the solvent completely surround the dried spot or stain. Then be careful not to move hastily or rub any of the clot loose. Only in this way is it possible to obtain a serum free from fibrin and blood corpuscles.

The mixture of the culture and serum may be observed in two ways: First, in the test tube; and, second, in the hanging drop. For the latter test are needed a microscope with a No. 3 or a No. 4 eyepiece, a one-sixth or one-seventh objective, hollow-ground slides, and absolutely clean cover slips (No. 1 or No. 2). Surround the hollow on the slide with vaseline or alboline, so that when the cover slip is placed over it its edges will be sealed, and thus evaporation will be prevented.

In the hanging-drop method, one drop of the fluid containing the bacteria, and one drop of the serum fluid are mixed on the cover slip and examined. In my experience the hanging-drop method is the most accurate if it be properly controlled. In the test tube the reaction is apparent to the naked eye, for when the organisms are clumped they collect at the bottom of the tube in a flocculent mass.

The clumping of the bacilli should take place in thirty minutes with a dilution of 1 to 20; if it takes more than thirty minutes or a dilution of less than 1 to 20, it should not be regarded in the light of a positive reaction, for it may then be due to a number of other factors which are too numerous to mention here. Some specimens of serum will not agglutinate in a dilution of 1 to 20, but will do so if the dilution be increased 1 to 50.

Instead of a clumping of the bacilli we may have what is known as a thread reaction; that is, the bacilli become arranged end to end, or, failing to separate completely as they multiply, they remain in the form of threads or chains.

The Distribution of the Typhoid Bacilli in the Body.—These organisms are found in the different tissues and fluids of the body as well as in the contents of the intestinal canal. We will consider these different localities in regular order, but in a very brief manner.

The Blood.—The typhoid bacilli are found with the greatest constancy in the blood. In the earlier examinations the search for these organisms in the blood gave very unsatisfactory results. At a later date, however, it was found that by the use of blood in bouillon highly diluted the presence of the bacilli could be demonstrated in the great majority of cases.

The Spleen.—Masses of the bacteria are found in the sinuses of the spleen, and splenic puncture has been recommended as a means of securing an early diagnosis. Such an exploratory puncture, however, is not free from danger to the patient, and the procedure is therefore not to be recommended.

The Rose Spots.—The bacilli may be obtained from these spots as early as on the seventh or eighth day apparently, in most instances, before the development, in the blood, of the substances which give rise to the Widal reaction (Hiss).

The Intestines and Their Contents.—It is here that the bacilli make their earliest appearance in the majority of cases. They are constantly found in Peyer's patches, and more particularly at the base of those which are ulcerated. They pass from these tissues doubtless by way of the lymphatics, and find lodgment in the mesenteric lymph nodes. Many of them are found in the phagocytic cells of the lymphatic system and also in the fixed phagocytic connective-tissue cells of the spleen. They are found also in large numbers in the fæces.

The Liver.—In this organ there have been observed small areas of degeneration, which have been termed focal necroses. They are caused by the lodgment of the bacilli at these points, and as these organisms grow their toxin causes a degeneration of the cells surrounding them. According to some reports the bacilli have been found in the gall bladder many years after an attack of typhoid fever, and it is even believed by some writers that they furnish a nucleus for the formation of gall stones. Bile often causes an agglutination of the bacilli.

The Kidneys and the Urine.—The bacilli have been demonstrated in the kidneys, and they are found in the urine in about twenty-five per cent. of the cases, but not before the fourteenth or fifteenth day of the disease; in fact, they are not to be found in the urine in some cases until convalescence is established. According to most observers the bacilli may persist in the urine for days or even weeks. It is even claimed by some authorities that they continue to be present in the urine for a period of several months.

The Mouth and Throat.—The finding of typhoid bacilli by Besson in the tonsils of six out of ten patients investigated warrants the belief that they also exist in the mouth.

The Lungs.—In some rare cases in which there has been a pneumonic form of infection, the bacilli have been found in the lungs. Indeed, in those cases in which an overwhelming blood infection—in other words, a septicæmia—occurs, they will be found in all the tissues of the body.

As the infection is not symmetrically distributed in all cases, there can be no one method of securing an early diagnosis. Hence, if he wishes to make a sure bacteriological diagnosis, the bacteriologist must take time, and it often happens that the clinician can be fairly certain of his diagnosis before he hears from the laboratory. Nevertheless, a bacteriological diagnosis is most important as a means of corroborating the clinical diagnosis.

Animals infected with B. typhosus have developed only in rare instances a disease at all comparable to that in man. So far as practical serum therapy is concerned, it has ever, in this disease, shown negative results.

Media Used as an Aid to the Isolation of the Bacillus Typhosus.—Many different media have been devised for use in isolating this organism, but there are only four which have stood the test of time, and which, in the hands of the trained bacteriologist, are admitted to be more or less effective in isolating the typhoid bacilli. The simplest one is that devised by Hiss. For completing the differentiation, however, Hiss uses two different media. His first step is to plate out some of the suspected material in a medium the composition of which is as follows:

Hiss' Plating Medium.

	Gm.
Agar	15.
Gelatin	15.
Liebig's extract	5.
Sodium chloride	5.
Dextrose	10.
Distilled water	1,000.

The agar is first melted and then the rest of the ingredients are added. After the mixture has boiled for a few minutes, it is allowed to cool and is cleared with the white of two eggs. Then it should be boiled again and filtered through a thin layer of absorbent cotton. Before filtering see that the total amount of fluid is 1,000 c.c.; and, if it be found to be less than this amount, add enough hot distilled water to bring it up to that point.

I have found that this is one of the most important points in making up this plating medium. No acid or alkali need be added to the mixture.

In this plating medium the typhoid colonies form thready growths, while the colon colonies are round with smooth edges. The colonies showing threads are fished out and plated in Hiss' tube medium, which is composed as follows:

Hiss' Tube Medium.

	Gm.
Agar	5.
Gelatin	80.
Liebig's extract	5.
Sodium chloride	5.
Dextrose	10.
Distilled water	1,000.

This medium differs from the first, as will be observed, in having 10 gm. less of agar and 65 gm. more of gelatin. The mixture is also cleared with the white of two eggs and is corrected to 1.5 acid, phenolphthalein being the indicator.

In this tube medium the Bacillus typhosus clouds it throughout in twenty-four hours. B. coli generally shows growth and gas formation only along the line of puncture. This medium has given us many excellent results, and I prefer it to all the others.

Elsner's Method (after Park).—1st. Grate 0.5 kgm. of small potates to a fine pulp and add one litre of cold water; let it stand over night in a cool place.

2d. Wash thoroughly and strain through a fine cloth. This must be done while the mixture is cold.

3d. Boil the filtrates and filter again.

4th. Add ten per cent. of gelatin and boil until it is dissolved.

5th. Test the acidity and have it so that 3 c.c. of a decinormal sodium-hydrate solution will neutralize 10 c.c. of the medium, phenolphthalein being the indicator.

6th. Boil and clear with egg.

7th. Filter through cotton and then through paper.

8th. To the filtrate add one per cent. of potassium iodide. (Use a solution so made that 1 c.c. shall contain 1 gm. of the salt.)

9th. Decant into tubes and sterilize.

The incubator for this medium must be kept at from 22° to 24° C.

The plates must be thoroughly cooled before placing in the incubator, as otherwise the difference between B. typhosus and B. coli would not be observed.

The colon colonies are the first to develop. They are rough and granular, and have a greenish-brown color; later, the typhoid colonies develop and are small, white, and gleaming, and can best be described as being dew-drop-like in appearance, although occasionally somewhat granular. This is apt to cause some confusion in the mind of the beginner, but one who is familiar with the use of this medium is very little likely to make a mistake. The potassium iodide prevents nearly all other organisms from developing in this medium.

This plating medium, used in conjunction with Hiss' tube medium, gives us a very satisfactory differential method.

The Capaldi plating medium and that formulated by von Drigalski and Conradi have in my hands furnished such variable results that I scarcely think it necessary to describe them here. The latter is a very complicated medium, by no means easy to prepare.

Distribution of the Bacilli Outside the Body.—The Bacillus typhosus may remain in contaminated soil for from two to three months, and in water for nearly the same length of time. On the other hand, if either the soil or the water contains enough organic matter for the support of the organism, it may remain there indefinitely.

The past few years have witnessed no change in our ideas regarding the transmission of typhoid fever. In fact, the theories of that time have merely been strengthened, and all are now agreed that in the vast majority of cases it is through the alimentary tract that the infection gains entrance to our system. In a few rare instances it is believed that the infection has been brought about by the inhalation of the Bacillus typhosus into the lungs.

There still remain to be considered the different methods by which this organism can gain entrance to the intestines. First, we may have a direct infection, that is, from a person suffering from the disease to one who has come in contact with the patient. When infection occurs in this manner some infected material must pass, through carelessness, to the alimentary canal of the individual contracting the disease; for, if perfect cleanliness and caution are observed, this form of infection need never occur.

Unless the excreta of the patient be thoroughly disinfected they will pollute the soil, and the infective organisms which they contain will remain quiescent until they are washed into some water supply, from which they gain entrance into some other human being. This may happen in any of the following ways: directly, as in drinking water or in ice, or in milk to which contaminated water has been added, either for purposes of dilution or in cleansing the receptacle. In milk the bacilli will multiply rapidly, unless the milk be kept constantly iced. If there be a large source of pollution, from which the polluted material drains into a river or creek, the submerged banks of which are used for the fattening of oysters, these will take in the bacilli and will furnish them, if decomposition should begin to develop in the host, with a soil most favorable for their rapid multiplication. It is under these circumstances that oysters may serve as the source of typhoid infection among those who eat them in an uncooked state. (At some later date the author proposes to publish the experiments which he has made in this special field.)

If the excreta be thrown into sinks and privies where flies congregate in large numbers, these insects will transfer the infected material to the house—*i.e.*, they will deposit it upon any food, cooked or uncooked, to which they may gain access. This is probably a frequent mode of spreading typhoid infection among the different members of a family after one of their number has been taken ill with the disease. Nothing short of the most thorough disinfection will prevent such a spreading of typhoid fever.

Raw vegetables may serve as carriers of the disease

provided they have been watered with infected material or have been washed in infected water, in preparation for their appearance on the table.

Ice cream, when manufactured of milk or cream which contains typhoid bacilli, and which has not been cooked, may serve to communicate the disease.

Major Firth, of the English Army Medical Corps, has recently shown that clothing which has been soiled by the excreta of a patient suffering with this disease may retain the virulent typhoid bacilli at the end of eighty-four days. Consequently soiled clothing, unless disinfected, may be a means of spreading the disease. The same authority has also shown that the bacilli may remain fully virulent in the soil for eighty-five days, and we know from other observations that it can remain so for much longer periods. Major Firth also claims that they may retain their virulence for twenty-five days after having been dried and blown about as dust. If this be so, it is certainly a matter of great importance, for it shows that the typhoid bacillus is a much more resistant organism than we have given it credit for being. This observation, however, must first be confirmed by other authorities before we can accept it as a fact.

To sum up, then, we find that there are three great roads by which infection reaches human beings. These are, first, personal contamination from person to person; second, contamination of water supply and therefore of milk and food; and third, the spread of the bacilli by household insects such as flies, cockroaches, etc.

From this it will be seen that the great weapons for combating the spread of this disease are, first, thorough disinfection of all excreta from the patient; and at this point I wish to emphasize the fact that it is of the greatest importance to disinfect and to handle carefully the urine of these patients. Our second weapon is the thorough sanitary supervision of our water supplies so that our water-sheds may escape contamination.

Cyrus West Field.

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VISION, DISORDERS OF: CHROMATOPSIA (*Colored Vision*).—Chromatopsia is a modification of the visual sensation, as a result of which all objects appear of a certain color (red, purple, blue, yellow, green, white), without any effect upon the acuteness of vision or any visible changes in the fundus.

Erythropsia (*Red Vision*), the most common variety, is not infrequent after cataract extraction, occurring in three to five per cent. of cases (Becker), and after exposure to intense light, for example, sunlit snow fields especially in high regions, brilliant electric light, flashes of lightning, and observation of the sun. This visual disturbance becomes more marked when the illumination is suddenly diminished, as after going from the open into a house. After cataract extraction there is less frequently purple or *blue vision* (*kyanopsia*), or the patient complains of objects appearing of a glaring white. The phenomenon generally appears shortly after the operation, or after some days or weeks; it lasts a variable number of hours, days, weeks, or months; it may be constant or intermittent; it generally disappears in the course of a few days or weeks. No treatment is called for beyond the wearing of smoke-tinted glasses; potassic bromide has been recommended in these cases.

Independently of cataract extraction, the occurrence of colored vision is favored by dilatation of the pupil, congenital coloboma of the iris, iridectomy, by excitement of any sort, and by elevation of body-temperature. Red vision is an occasional symptom of optic-nerve atrophy, glaucoma, nyctalopia, migraine, hysteria, hystero-traumatic amblyopia, and amaurosis, exhausting diseases, and severe fevers; it sometimes occurs with intra-ocular hemorrhage; it may be part of the epileptic aura; it is said to be caused by coffee in rare instances. Blue vision is occasionally complained of by patients suffering from retinitis albuminurica and detachment of the retina, and may also follow the use of cannabis indica. *Green vision* (*chloropsia*) is a rare symptom of detachment of the retina, optic-nerve atrophy, and aphakia as the result of cataract extraction. Blind eyes occasionally are conscious of colored lights, probably due to irritation of the visual centres.

It seems probable that chromotopsia may be due either to central irritation or to local causes. No entirely satisfactory explanation of the phenomenon has yet been offered. Fuchs attributes red vision to the action of strong light on the visual purple and its slow regeneration under less intense light; but the absence of visual purple at the macula upsets this theory. Snellen believes it to be due to the coloring of white light by its passage through the translucent and vascular lids and choroid, and the subsequent diffusion of this reddish light over the retina. After the extraction of cataract, upon exposure to bright light, the lids are partly closed; there is thus a small central pupillary opening for white light, while the periphery of the retina is flooded with red light which has come through the lids. When the intensity of the illumination is reduced, the red perception of the periphery changes to a complementary green as a result of fatigue, while central vision appears red by contrast. The blue vision after cataract extraction is attributed by Burnett to fatigue of the retina as a result of long-continued exposure to light rendered yellow by passage through amber-colored cataracts, giving blue as a residual sensation in white light.

Toxic Chromatopsia.—Colored vision, usually yellow (*xanthopsia*), is one of the symptoms of the poisonous effects of certain drugs, of which santonin is the most common example; this agent may, however, produce green vision, or rarely red or blue vision. Other drugs which may produce chromatopsia are amyl nitrite, picric acid, chromic acid (as a result of local applications), osmic acid, digitalis, carbonic oxide, and tobacco. Xanthopsia also occurs as an early symptom of catarrhal jaundice, being due probably to the discoloration of the dioptric media and the structures of the eyeball by bile pigment. Yellow vision is also seen after dazzling from electric light, and occasionally accompanies nyctalopia.

Charles H. May.

WOLFFIAN BODY, PATHOLOGY OF.—In mammalian embryos the mesonephros or Wolffian body is a rather pyriform body symmetrically placed in the abdominal cavity. In very young embryos it is, next to the liver, the largest abdominal organ. It was first observed by Wolff in 1759. The exact origin of the Wolffian body is not yet determined; some authors hold that it is ectodermal, others that it is mesodermal, while others still ascribe to it both an ectodermal and a mesodermal origin. It is developed from the pronephric or Wolffian duct and from the mesonephric cords. The origin of the latter has not yet been wholly worked out in the case of the human body. In the lower mammals they arise through aggregations of the cells of the Wolffian ridge into solid cords which at first are not connected with the Wolffian duct or the cœlomic epithelium. These cords acquire a lumen and connect at one end with the duct, while at the other end there is a condensation of the mesoderm, forming the glomeruli, into which vessels from the aorta penetrate. The tubules increase in length rapidly and in the human embryo assume an S-shape. Secondary and tertiary tubules develop in connection with each of the primary ones, but the mode and origin of these have not yet been determined, some writers hold-

ing that they arise as buds of the primary tubules, others that they have an independent origin. Through the development of these additional tubules and the progressive elongation of all the tubules, the Wolffian ridge becomes a voluminous body attached to the dorsal wall by a distinct mesentery and projecting into the cœlomic cavity. Embedded in its substance on its lateral portion is the Wolffian duct; and on its mesial surface anteriorly is the developing genital ridge. In the human embryo the Wolffian body reaches its greatest development at about the sixth or seventh week, after which time it begins to degenerate. The tubules undergo retrogression and the glomeruli become occluded, so that by the sixteenth week the organ has nearly entirely disappeared. Portions of the tubules, however, persist in both sexes. In general the tubules of the Wolffian body consist of

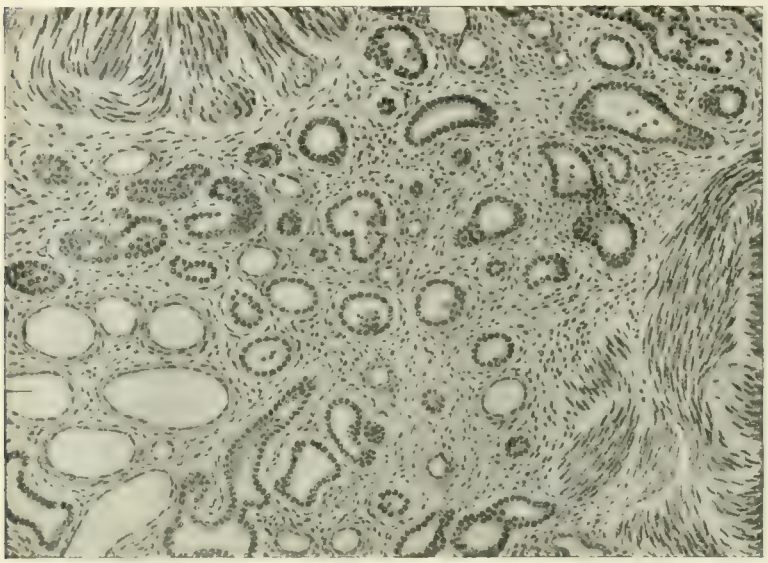

FIG. 5246. Adenoma-like Remains of the Wolffian Body, within the Uterine Musculature (formalin, alcohol, hæmatoxylin, eosin). × 100. (After Ziegler.)

secreting and collecting portions, the epithelium varying in the two, being low and cubical in the collecting portion and columnar in the secreting. In 1824 Jacobson discovered that the organ excreted uric acid which was carried into the allantois. He therefore called it the primordial kidney. According to Lorsel the Wolffian body liberates and accumulates fatty substances in its cells. It therefore plays the part of an embryonic organ and at the same time that of an excretory organ.

In the male the upper or genital portion of the Wolffian body persists as a whole in the efferent ducts of the testis, forming the globus major of the epididymis. By some writers the seminal tubules are also regarded as arising from the Wolffian body. The excretory portion almost wholly disappears, only a small part remaining as the paradidymis or organ of Giraldès. A single elongated tubule arising from that portion of the Wolffian duct which forms the globus minor of the epididymis persists as the vas aberrans. The hydatid of Morgagni is believed by Roth to stand in close relation to the Wolffian body. The Wolffian duct is retained entire, a portion forming the body and globus minor of the epididymis, the remainder becoming converted into the vas deferens and the ejaculatory duct. In the female the genital portion of the Wolffian body persists as a group of from ten to fifteen tubules lying between the two layers of the broad ligament near the ovary, and known as the epoöphoron, or parovarium, or organ of Rosenmüller. Toward the ovary the tubules possess blind ends, but at the other end they are somewhat coiled and open into a collecting duct representing the upper end of the Wolffian duct. Kölliker holds that the environing cells of the Graafian follicle probably arise from the Wolffian body. The excretory portion persists as the paroöphoron, a rudimentary body composed of tubules lying in the broad ligament near the tube. In about one-third of adult females remains of the Wolffian duct are found in the form of a straight tube lined by cylindrical epithelium surrounded by muscle, or of a muscle bundle without epithelium, lying anteriorly and to the side of the uterus and vagina (duct of Gärtner). According to Aichel the cortex of the suprarenals is also derived from the Wolffian body, the medullary portion coming from the sympathetic system. The origin of suprarenal tissue from the Wolffian body is made very probable from the fact that accessory suprarenal tissue (adrenals of Marchand) is found in the broad ligament in the female, and along the spermatic cord and near the epididymis in the male.

Of the pathological conditions directly affecting the Wolffian body we know nothing at present. Hyperplasia of the primitive Wolffian body has been assumed, but not yet demonstrated. It is, however, very probable that disturbances in the development and retrogression of this organ are responsible for a number of important pathological conditions which are either apparent at birth or develop later in life. From the rudimentary structures which represent persisting portions of the Wolffian body and duct there may develop tumors of great clinical importance. Of the factors concerned immediately in the genesis and development of these tumors nothing is yet known. In general the pathological conditions which may be referred back to disturbances in the normal development and retrogression of the Wolffian body, or which have their origin in rudimentary or persisting structures derived from this organ or duct, may be classed as follows:

Malformations.—The fact that both male and female sexual organs, internal and external, develop from anlage which are at first identical makes it *a priori* very probable that disturbances in the differentiation of the sexual apparatus might be brought about through an asymmetrical development of the anlage of the right and left sides, or through the formation of organs peculiar to both sexes, or to a lack of harmony in the development of the internal and external sexual organs. The close relations between the Wolffian body and the developing sexual glands, and the part which the genital portion of the former plays in the development of the genital tract give strong support to the view that anomalies and disturbances in the development of the mesonephros are responsible, at least in part, for some of the malformations of the internal sexual apparatus. Landau and Pick have described a congenital atresia of the cervix and uterus, which they explain as due to a hyperplastic adenomyoma of mesonephric origin. Persistence of portions of the Wolffian body and duct are not infrequently found in cases of pseudohermaphrodism. In pseudohermaphrodismus femininus internus such structures are found in the broad ligament and utero-vaginal wall, sometimes extending to the clitoris. At an early period of development the urogenital tract is represented by the Wolffian body, the Wolffian duct, the Müllerian duct, and the developing ovary or testis. There exists therefore at this time an indifferent stage from which the development proceeds either in one direction to become an ovary or in the other to form a testis. During this differen-

tiation the Wolffian body in part undergoes degeneration and in part persists in the form of certain rudimentary organs, as already mentioned. In the male the Müllerian duct degenerates, in the female only rudiments of the Wolffian duct are preserved. Theoretically it is easily seen how disturbances of this normal differentiation of the sexual glands and ducts might arise, but the actual occurrence of such disturbances remains to be demonstrated, although pathological findings are not wanting to prove the possibility of such.

Teratomata and Dermoid Cysts.—The teratomata and dermoid cysts of the ovary and testis are believed by a number of writers to arise from the Wolffian body and duct. Bandler in particular has defended this view. He holds that in the development of the retroperitoneal dermoid cysts and the retrorectal tumors the Wolffian body, the Wolffian duct, and the caudal intestine play the important rôle. The ovarian dermoids, he believes, contain only ectodermal and mesodermal products, and these arise as the result of the displacement of ectodermal and mesodermal tissues in the formation of the Wolffian duct and Wolffian body. Regarding the duct as of ectodermal origin, and holding the view that the Wolffian body arises from the duct, he therefore regards the derivatives of the Wolffian body as ectodermal. While Bandler's views are not generally accepted (see *Teratoma*), Wilms regards the simple dermoid cysts of the retroperitoneal region and of the broad ligament, and also the mixed tumors of the cervix and vagina, as due to a displacement of ectodermal and mesodermal cells by the Wolffian duct. Von Recklinghausen found in one cyst of the ovary a formation which he regarded as resembling in structure the Wolffian body. The cysts which arise from the remains of the Wolffian body and duct found in the broad ligament, uterine wall and tubes, and also those arising in the cervix, portio vaginalis, vagina, and hymen from the duct of Gärtner may also be classed with the teratomata. Remains of the Wolffian body may also take part in the formation of the mixed tumors of the kidney. If the view that adrenal tissue is also derived from the Wolffian body be accepted the tumors (hypernephromata) arising in the kidney and elsewhere should also be classed as teratomata derived from the Wolffian body.

Tumors Derived from Wolffian Body Rests.—During the last decade much has been written upon the origin of the adenocystomata and adenomyomata of the ovary, broad ligament, tube, uterine wall, cervix, and vagina. These tumors play a rôle of great clinical importance in gynæcological pathology, and in recent years much attention has been paid to their histogenesis and etiology. As a result of the discussion concerning the histogenesis of these tumors the writers upon this subject may be divided into two schools: the one affirming the origin of these growths from remains of the Wolffian body, the other holding that they arise from misplaced epithelium of Müller's duct. Some writers have compromised, in so far as the adenocystomata and adenomyomata of the uterine wall are concerned, by the hypothesis that they arise from a combination of remains of the Wolffian body and the Müllerian duct. The majority of writers, however, agree with von Recklinghausen, who holds that the adenomyomata of the uterine wall may be divided into two groups: those arising in the peripheral layers of the myometrium and those arising centrally or presenting themselves as submucosal tumors, the latter being characterized by the fact that the adenomatous portions unite to form ducts which empty into the uterine cavity. The possibility of the second group arising from the Müllerian duct is admitted. According to Neumann the intramural and subserous adenocystomata of the uterus and tubes arise most probably from embryonal remains of the Wolffian body in connection with remains of Müller's duct or from a combination of the two. The pathological glands and cyst formations found in the ovary arise from the epoöphoral portion of the Wolffian body and correspond to the medullary cords. The tumors of the tubes are of pure paroöphoral origin. The structural resemblances existing between the adenomyomata of the ovary, tubes, broad ligament, inguinal region, round ligament, and cervix, make it very probable that all of these are derived from the Wolffian body, and they may therefore be classed as mesonephric adenomyomata. The various arguments advanced in support of this view may be found in the literature cited below.

The adenosarcomata of the kidney have also been explained as arising from inclusions of portions of the Wolffian body. A similar origin has been ascribed to the adenosarcomata, adenomata, and adenocystomata of the testis and epididymis. Some writers have described glandular structures included within pelvic lymph glands, and have explained such inclusions as remains of the Wolffian body or duct. From such inclusions adenomata, cystadenomata, and carcinomata might arise.

To Aichel belongs the credit of demonstrating that adrenal tissue (cortex) is found in the closest relations with derivatives of the Wolffian body (epoöphoron, paroöphoron, epididymis, paradidymis, broad ligament, etc.). From such accessory adrenal tissue (classed by Aichel as adrenals of Marchand) tumors similar to those arising from the adrenals themselves may come. Pick has reported the occurrence of a hypernephroma of the ovary, and a number of other writers have found adrenal tissue associated with adenomyomata. If the adrenals of Marchand are derived from the Wolffian body, as according to Aichel, such hypernephromata must be regarded as mesonephric. *Aldred Scott Warthin.*

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WORMIAN BONES, AND FONTANELS.—Wormian bones are small bones varying in diameter from 1 or 2 mm. to more than 20 mm. They are to be found ordinarily at the angles of the sutures of the cranium, and particularly in the lambdoid sutures (Fig. 5248). They take the name of Wormian bones from Claus Wormius, a physician of Copenhagen, who first gave a detailed description of them, though an account of them had been given before by Gœthes.

The Wormian bones are regarded by some writers as evidence of retarded ossification, while by others they are considered to indicate excessive ossification. Doubtless both theories are true. In some instances the usual centres of ossification do not go on to the full development, and the coalescence which occurs in the formation of a perfect bone fails to take place; this is probably what happens in the case of the largest Wormian bones, which are found in the fontanels.

According to Meckel, isolated osseous germs develop

FIG. 5247. Wormian Bones. (After Broca.)

at the circumference of the occipital bone and unite themselves with it. Sometimes, though rarely, thicker ones develop about the articular regions. When there is an arrest of evolution of one or more of these inferior centres, Wormian bones are formed. Gosse, who considers Wor-

mian bones to be due to an arrest of ossification, attributes their formation to a rachitic or scrofulous condition, to the effects of violent pressure, or to hereditary transmission.

The Wormian bones which present the greatest interest are those which are occasionally found in both the

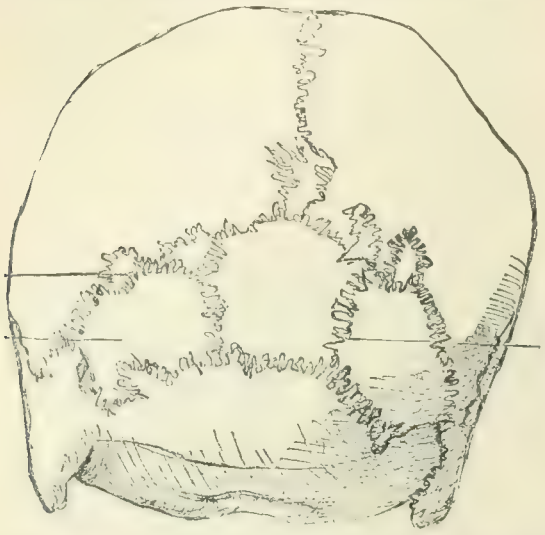

FIG. 5248. Skull dug up in the Vicinity of the Church of St. Etienne du Mont. (After Jacquart.)

anterior and posterior fontanels. Those in the posterior fontanels are more frequent (Figs. 5248 and 5249). A Wormian bone of large size may be confounded with the interparietal bone, which has given rise to so much ethnological discussion; a number of interesting and learned papers having been written by anthropologists upon this subject. M. Rivero and M. Tschudi, in the "Antiquités Péruviennes," published in 1851, gave drawings showing the bone which Anoutchune, after making studies of the skulls in various museums, announced was to be found in twenty per cent. of the Peruvian skulls. The name, "the bone of the Incas," was given to it, though,

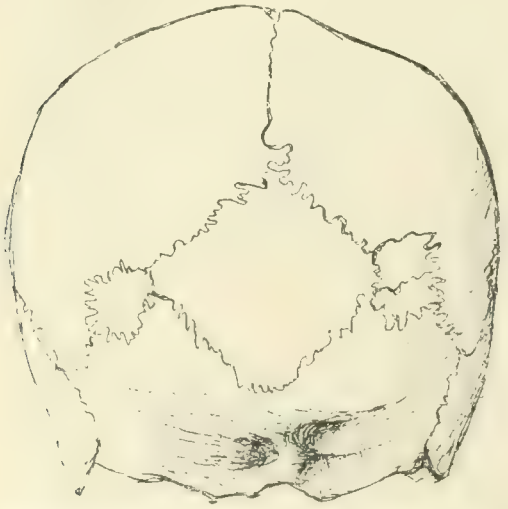

FIG. 5249. Skull of a Negress of Sahara. (After Jacquart.)

as Jacquart thinks, unjustly. In an elaborate paper he shows that it is found frequently in other races. The question among savants has arisen as to whether this is a mere anomaly, or a reversal to a lower type, since the interparietal bone occurs in rodents, ruminants, dogs, and cats. The upper portion of the occipital bone develops from four osseous centres, which are separate in early fœtal life, but gradually coalesce. The lateral union is accomplished first, and afterward the two segments above and below unite; when union of these two latter fails to take place, the interparietal bone is formed. The recent line of union shows very well in the skull of the new-born. Cuvier, Milne-Edwards, Geoffroy St. Hilaire, and the other writers already mentioned, insist that a distinction should be made between the interparietal bone and the large fragments occurring in the posterior fontanel, which are the true Wormian bones. Anoutchune, in his researches, made the following divisions in summing up his percentages:

1. Complete: Os Incas, or interparietal bone.
2. Incomplete: The os bi-, tri-, or quadripartitum, or, in other words, the epactal bone, os triquetrum, os quadratum.
3. Os lambdoideum.

It will therefore be seen that these bones may be single or multiple; even as many as eight having been observed by one writer quoted by Geoffroy St. Hilaire.

The effect of Wormian bones occurring in fontanels at childbirth, and the relation which these bear to the

FIG. 5250. Skull from a Breton, showing Interparietal Bone. (After Jacquart.)

moulding of the skull at that time, are questions which have received some consideration by the author of this paper.

The possibility that such bones, if of considerable size and if they occurred in the posterior fontanel, might exert a detrimental, if not fatal, influence, was suggested by three cases which came under observation at the hospital of the New York Infirmary for Women and Children. The histories of the three cases were almost identical. The mothers were all primiparæ. There was nothing abnormal in the measurements, either of the pelves of the mothers, or of the heads of the infants. The presentations were all of them the usual left anterior occipito-iliac. The labors progressed slowly but normally through the first stage, but the second stage was very slow, lasting between two and three hours in each case. Instruments were not used in any instance, as there was a constant expectation that the labors would terminate naturally. The irregularity of the fontanel could be very easily detected. In the first two cases it gave rise to confusion in determining the position; but in the third and last case, the attendant, having had the experience with the two others, easily discovered that the posterior fontanel contained Wormian bones (Fig. 5251). Each child was still-born. The skulls of two were preserved, but

the family would not permit an autopsy to be made upon the third child, which was taken away for burial. It could, however, be easily felt that Wormian bones were

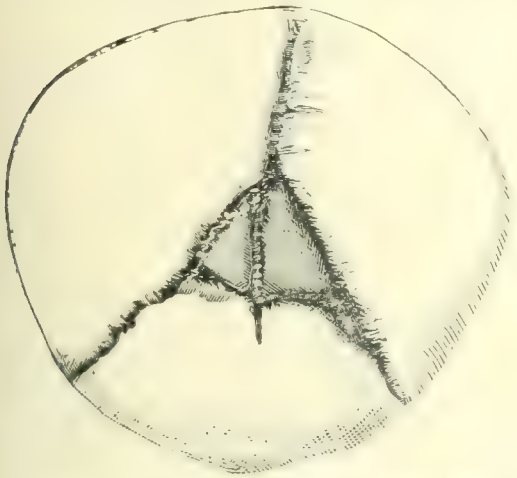

FIG. 5251.—Wormian Bones, as seen in the Author's Case.

present and that their shape and number were the same as in the other two cases, there being two triangular pieces, one larger than the other.

The writer believes it to be possible that during labor these bones may prevent the usual overlapping of the sutures of the skull, and that during the second stage—*i.e.*, when the pressure is greatest—they may even inflict serious, possibly fatal, injury upon the contents of the cranium. The question then arises, Could this be avoided by the prompt and early use of instruments? It is hoped that obstetricians will record cases of a like nature, and report upon them with a view of determining the effects produced by Wormian bones during the progress of childbirth. *Grace Peckham Murray.*

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YELLOW FEVER: HISTORY AND GEOGRAPHIC DISTRIBUTION.—The geographical range of yellow fever is more restricted than that of any other acute infectious disease, and within the area of its prevalence it is essentially a disease of the littoral, and especially of seaport cities. While occasional epidemics have occurred upon the southwest coast of the Iberian peninsula, the disease, as an epidemic, is unknown elsewhere in Europe, and there is no evidence that it has ever invaded the great and populous continent of Asia. In Africa it is limited to the west coast. In North America, although it has occasionally prevailed as an epidemic in every one of our seaport cities as far north as Boston, and in the Mississippi Valley as far north as St. Louis, it has never established itself as an endemic disease within the limits of the United States. Vera Cruz, and probably other points on the gulf coast of Mexico, are, however, at the present time, endemic foci of the disease. In South America it has prevailed as an epidemic at all of the seaports on the gulf and Atlantic coasts, as far south as Montevideo and Buenos Ayres, and on the Pacific along the coast of Peru.

The region in which the disease has had the greatest and most frequent prevalence is bounded by the shores of the Gulf of Mexico, and includes the West India islands. Within the past few years yellow fever has been carried to the west coast of North America, and has prevailed as an epidemic as far north as the Mexican port of Guaymas, on the Gulf of California.

The idea that yellow fever may originate *de novo*, within the area of its occasional prevalence, was entertained by many medical authors during the first half of the past century. Thus Cornillac (1886) says: "In the zone which is habitual to it, yellow fever may develop at a given moment without apparent cause. It is born spontaneously at a point of this zone, or at several at a time, and neither the temperature, moisture, barometric pressure, electricity, nor finally effluvia given off from the soil, can explain this sudden invasion." It is true that, in localities where the disease is endemic, cases occur which are not directly traceable to importation, but it is also true that in the principal endemic foci of the disease, such as Vera Cruz, Havana, and Rio Janeiro, yellow fever was at one time unknown, and we have reliable historical data fixing the date of its importation. In short, a careful consideration of the historical evidence relating to the disease gives no support to the idea of independent local origin, any more than in the case of smallpox, cholera, or other specific infectious diseases.

But the early history of the disease is involved in obscurity, and we are at present unable to determine whether, as maintained by some, it was endemic at certain points on the shores of the Gulf of Mexico at the time of the discovery of the "new world," or whether it was imported to the West Indies from the African coast, as maintained by others. The early historians, Herréra, Oviédo, Rochefort, and others, make reference to epidemics among the natives which occurred prior to the discovery of the Antilles, and to fatal pestilential diseases among the first settlers of these islands; but their accounts are not sufficiently exact to enable us to affirm that the disease referred to by them was yellow fever. The west coast of Africa was discovered and colonized to some extent before the discovery of America, but the first authentic accounts of the prevalence of yellow fever on this coast date back only to the year 1778, over two centuries after the first settlements had been established. On the other hand, this very epidemic of 1778 at St. Louis (Senegal) was traced to importation from Sierra Leone, a portion of the African coast which, according to Hirsch, "appears to be the headquarters of the disease, and the starting-point of its epidemic inroad into the territories lying to the north and south, as well as into the West African islands."

Rochefort, whose "Histoire naturelle et morale des isles Antilles de l'Amérique" was published in Holland in 1558, says of the West Indies: "The air of all those islands is very temperate, and healthy when one is accustomed to it. The *peste* was formerly unknown there as well as in China and other places in the Orient; but some years since the islands were afflicted with malignant fevers, which the physicians considered contagious. The bad air was brought there by some ships which came from the coast of Africa, but at present we hear nothing more of these maladies."

It seems very probable that a pestilential malady which prevailed for a time in these usually healthy islands and then disappeared was in fact yellow fever, and that it was introduced by ships from the west coast of Africa is not at all incredible. Indeed, it almost seems necessary to look for an original endemic focus of the disease outside of the West Indies, for the reason that, in the comparatively few places where it is now endemic, there is historical evidence to show that there was a first importation and a previous period of exemption; while, on the other hand, the conditions upon which endemicity at the present day seems mainly to depend were formerly unknown—conditions arising from the aggregation of population at seaport cities, as at Havana, Vera Cruz, and Rio Janeiro.

Some authors have attempted to identify the epidemic disease mentioned by Humboldt—called by the natives "Matlazahuatl"—which prevailed in Mexico in 1545, 1576, 1736–37, and 1761–62, with yellow fever; but, as pointed out by Hirsch, this disease prevailed almost exclusively among the natives of the interior and of the tableland of Mexico, while yellow fever is essentially a disease of the littoral.

Cornillac, a French author who has made a careful study of the sanitary history of the West Indies, as contained in the works of Oviédo, Herréra, Gomara, and other Spanish authors of the sixteenth century, arrives at the conclusion that the pestilential disease from which the settlers in the first Spanish colony at Nueva-Isabella, and at Santo Domingo (1494–1514), are said to have suffered, and which was characterized by a "saffron-yellow" color of the skin, was in truth yellow fever. While it appears quite probable that this was so, we cannot accept it as demonstrated, as the first authentic accounts of yellow fever in the West Indies date from about the middle of the following century.

In 1635 a French colony was established upon the island of Guadeloupe, and shortly after their arrival a pestilential disease appeared among the colonists which, from the account given by Dutertre, a Catholic priest who came to the island five years later, is accepted by Hirsch and by Cornillac as having been yellow fever. From Dutertre's account, however, as quoted by Cornillac, it would appear that yellow fever was first imported into the island of Guadeloupe in the year 1648, and that the great mortality previously reported was due to other causes. Dutertre says: "During this same year 1648, the *peste*, until then unknown in these islands since they were inhabited by the French, was brought there by some vessels. It commenced at Saint-Christophe, and during the eighteen months that it lasted carried away nearly one-third of the inhabitants. This epidemic *peste* caused in those who were attacked a violent *mal de tête*, great debility in all the members, and continual vomiting, so that in three days it put a man in his tomb. This contagious malady was brought to Guadeloupe by a ship from La Rochelle, called *Le Bœuf*."

At Barbadoes the disease may have prevailed for some years prior to its introduction into Guadeloupe, but the first authentic account relates to the year 1647. Richard Ligon, who arrived at the island in the month of September of this year, says that the city of Barbadoes was at that time suffering from a scourge which caused great ravages, so that the living scarcely sufficed to bury the dead. According to this author, the cause of the epidemic was unknown; it was uncertain whether it had been imported, or whether it originated from bad food, the use of marsh water, and the intemperance of the colonists. Ligon inclines to attribute it largely to the latter cause, and remarks that not more than one woman died for every ten men. We may safely assume, from the subsequent history of the island of Barbadoes, that the epidemic plague referred to by Ligon was not of local origin, for, with a rapidly increasing population this island has enjoyed considerable periods of immunity from yellow fever, and when epidemics have occurred they have, as a rule, been clearly traced to importation. From this time—1647–48—the history of yellow fever in the West Indies is a history of epidemic outbreaks at varying intervals, at the principal seaport towns, traced sometimes to importation, but more commonly assumed to be of local origin. It was epidemic in Jamaica in 1655, and again in 1671; at Santo Domingo in 1656; at Martinique in 1688 and 1696. In 1699 it prevailed widely as an epidemic in the West Indies, and, according to Hinemann, made its first appearance at Vera Cruz, the principal seaport on the gulf coast of Mexico.

Cuba.—I cannot attempt to follow here the history of yellow fever in the West Indies generally, but shall give an account of its prevalence in Havana.

The historian Pezuela records the prevalence of a malignant pestilential disease in Havana in 1648, a year in which, as we have seen, yellow fever was epidemic in the islands of Guadeloupe and of Barbadoes. He says: "In this year there occurred in Havana a great pest of putrid fevers which remained in the port almost all the summer. A large part of the garrison and a larger part of the crew and passengers in the vessels died." The epidemic continued the following year, and in 1653–54, according to the author above quoted, "the epidemic was renewed with equal fury"; and in 1655 "in the capital continued to carry away its victims without regard to rivalries and passions." According to Dr. S. E. Chaillé, president of the Havana Yellow-fever Commission (1879), from whose report we have quoted the above extracts from Pezuela, there is no historical evidence of the prevalence of yellow fever in Havana for more than a hundred years after the date mentioned. "On the contrary, there are repeated records of the great salubrity of the climate and the absence of epidemic diseases."

It was not until the year 1761 that yellow fever established itself in the previously healthy city. Pezuela gives the following account of its introduction: "Although Havana is situated on the northern boundary of the torrid zone, it was very justly considered one of the most healthy localities on the island before its invasion, in a permanent manner, by the *vomito negro*, imported from Vera Cruz in the summer of 1761. . . . In May there came from Vera Cruz, with materials and some prisoners destined for the works on the exterior fortifications of Havana, the men-of-war *Reina* and *America*, which communicated to the neighborhood the epidemic known by the name of 'vomito negro.' At the end of the following June there were stationed in this port nine men-of-war, despatched from Cadiz, and sent to the chief of the squadron, Don Entienne de Hevia; they brought a reinforcement of 2,000 men. More than 3,000 persons succumbed to the epidemic on this *the first appearance* of the vomito."

From this time the new levies of troops sent from Spain to Cuba continued to suffer enormous losses from the endemic pestilence. In 1779 there arrived from Spain, then at war with Great Britain, "an army of 3,500 men, which was immediately decimated by the vomito." In 1780, during the month of August, an army of 8,000 men was landed in Havana, which during the two following months suffered a loss of about 2,000 men with the vomito. Pezuela records the fact that in 1794, in the garrison and squadron, there were more than 1,600 victims to the disease.

The endemicity of yellow fever in Havana was fully established by the reseaches of the commission sent to that city in 1879, by the National Board of Health. Dr. Chaillé, president of this commission, says in his elaborate report, published in 1881: "Since 1761 yellow fever has prevailed certainly in Havana, and probably in other places in Cuba, every year, and the dates of prevalence recorded in our text-books indicate no more than the years of greatest prevalence. The disease prevails in Havana, and in some other places in Cuba, not only every year, but also every month in the year; records in 1837 indicate that at that date the monthly prevalence had become habitual in Havana; the statistics, solely of the military and civil hospitals, prove that during the 408 months, 1846–79, there was only one

single month free from officially recorded cases of yellow fever."

The following tables are from the "Preliminary Report of the Havana Yellow-fever Commission":

MONTHLY MAXIMUM AND MINIMUM DEATHS BY YELLOW FEVER IN HAVANA DURING THE TEN YEARS 1870-79.

Months.	Minimum.	Maximum.	Months.	Minimum.	Maximum.
January	6	32	July	68	675
February	4	24	August	70	416
March	4	32	September	35	234
April	4	37	October	28	185
May	13	103	November	5	150
June	66	378	December	9	82

In no one of the ten years 1870–79 have there ever been fewer deaths than in the first, nor more than in the second, column, and the total deaths by yellow fever for each year were as follows:

TOTAL DEATHS BY YELLOW FEVER IN HAVANA.

In 1870	665	In 1875	1,001
In 1871	991	In 1876	1,619
In 1872	515	In 1877	1,374
In 1873	1,244	In 1878	1,559
In 1874	1,425	In 1879, to Oct. 1st	1,353

The disease continued to prevail in Havana up to the time of the occupation of that city by the United States troops in 1898. According to Colonel Gorgas the mortality during the month of October between the years 1889 and 1899 ranged from 25 in 1899 to 240 in 1896 (average for ten years 66.27). After the demonstration by Major Reed and his associates (1900) that yellow fever is transmitted through the agency of mosquitoes, Colonel Gorgas (then Major Gorgas, surgeon U.S.A.) inaugurated his successful campaign against infected mosquitoes, and in November, 1901, was able to report that: "During the month we have had no cases and no deaths from yellow fever. Last year, 1900, we had during this month 214 cases and 54 deaths. This year the last case occurred on September 28th, that is, we have gone over two months without a single case or death belonging to Havana." This record has been continued since, and the city of Havana has ceased to be one of the endemic foci of the disease under consideration.

The board for the study of yellow fever in the island of Cuba was appointed upon my recommendation and received its instructions from me. It was constituted as follows: Major Walter Reed, surgeon U.S.A., Dr. James Carroll, contract surgeon U.S.A. (now assistant surgeon U.S.A.), Dr. A. Agramonte, contract surgeon U.S.A., and Dr. Jesse W. Lazear, contract surgeon U.S.A. The demonstration that yellow fever is transmitted by infected mosquitoes was made during the summer of 1900 and announced in a "Preliminary Note" read at the meeting of the American Public Health Association, October 22d, 1900. The conclusions of this board have been fully confirmed by the commission sent by the French Government in 1901 to investigate yellow fever in Rio Janeiro. This commission found that the blood serum of yellow-fever patients is virulent up to the third day of the disease, but not later. The virus passes with the serum through a Chamberlain filter (bougie F). This is in accord with the results obtained by Major Reed and his associates, who found that blood serum from a yellow-fever patient, obtained during the first three days of the disease, when passed through a Berkefeld filter still contains the specific infectious agent, as proved by successful inoculations in susceptible individuals.

These results are in accord with my own conclusions, reached after extended investigations made in Cuba, in Brazil, and in Mexico (in 1878, 1887, 1888, and 1889). In my final report I say:

"The specific cause of yellow fever has not yet been demonstrated.

"It is demonstrated that micro-organisms capable of development in the culture media usually employed by bacteriologists, are only found in the blood and tissues of yellow-fever cadavers in exceptional cases, when cultures are made very soon after death."

The inference from filtration experiments considered in connection with the fact that it has not been possible to demonstrate the presence of a specific micro-organism in the virulent blood of yellow-fever patients appears to be that the germ of yellow fever is so minute as to be ultramicroscopic.

Yellow fever prevailed almost annually in some of the other seaports of the island of Cuba prior to the American occupation of that island, especially in Matanzas, Cienfuegos, Santiago de Cuba, and Manzanillo.

Vera Cruz, the principal seaport on the gulf coast of Mexico, is also the principal endemic focus of yellow fever upon this coast. According to Hinemann, the first epidemic occurred in 1699, a year in which yellow fever was widely prevalent in the West Indies, and in which it prevailed for the first time as an epidemic in the city of Philadelphia.

The following table, which I copy from a paper by Dr. Zacarias R. Molina, a medical officer of the Mexican army who has for a number of years been on duty in the Military Hospital at Vera Cruz, shows the continued prevalence of the disease in that city during a period of nearly fifteen years:

MORTALITY FROM YELLOW FEVER IN THE CITY OF VERA CRUZ FROM JULY, 1867, TO DECEMBER, 1881.

Months.	1867	1868	1869	1870	1871	1872	1873	1874	1875	1876	1877	1878	1879	1880	1881	Total
January		7			3	2	1	1	7			16	6	2	28	
February		6				2		2	2	1	1	5	4		22	
March		7			1	4			4	1			2	1	29	
April		31	2		6	5	3		11			1	1	1	29	
May		42			19	14	1	2	29		4	7	1		94	
June		16			113	45	19	3	93	2	7	58	1		233	
July	8	28	1		71	53	59	11	118	4	54	114	2	1	132	
August	29	21	1		17	39	59	24	105	7	114	110	1	3	39	
September	36	21			10	29	74	7	41	9	166	62	3	9	32	
October	17	9	1	3	15	11	20	12	13	6	77	45		42	25	
November	11	2	2	5	2		10	11	2	1	50	24		92	18	
December	8	3		2	4	6	7	6		3	27	7		98	4	
Totals	109	193	7	10	271	210	223	79	425	34	528	444	21	249	675	

There is no evidene of continued prevalence at other towns upon the Mexican Coast, but epidemics, which have usually been traced to importation from Vera Cruz, have occurred at *Matamoras*, at *Tampico*, at *Tuxpan*, at *Campêche*, and at *Manzanillo*.

The gulf coast of South America, and especially the English and French settlements in Guiana, have been frequently visited by epidemics of yellow fever, and it is probable that the disease is endemic at one or more points upon this coast. Its epidemic prevalence is recorded for the following years at *Demerara:* 1793–96, 1800, 1803, 1818, 1819, 1820, 1821, 1825, 1827, 1828, 1831, 1837–39, 1841–45, 1851–53, 1861–66 (Hirsch).

In Venezuela the disease has prevailed at the capital, *Caracas*, and the neighboring seaport, *La Guayra*.

In Central America epidemics have occurred at all of the principal seaports: *Panama*, *Portobello*, *Belize*, *Nicaragua*.

BRAZIL.—The Portuguese author El hastião da Rocha Pitti has given an account, in his "History of Portuguese America," published in Lisbon in the year 1730, of an epidemic malady which prevailed in Pernambuco in the year 1686, which very probably was yellow fever. This author says (Book VII., p. 427 *et seq.*): "In the year 1686, commenced in Pernambuco that terrible plague (contagious disease, *Bicha*) which must be attributed to the sins of the population of these provinces, corrupted by the vices into which they were enticed by the wealth and freedom of Brazil. Many causes are alleged, the most worthy of attention being the arrival of some barrels of meat which returned from the island of São Thomé (St. Thomas). These were opened by a cooper,

who shortly afterward fell dead. Soon after several persons of his family, to whom he had communicated the disease, also died. The epidemic spread to such an extent among the inhabitants of Recipe (Pernambuco) that the mortality exceeded two thousand, which was very large in proportion to the population. Thence the disease extended to Olinda and its vicinity, and very few were the persons who escaped it, such were its virulence and intensity." The account given by the historian of the clinical features of this pestilential disease is, of course, very imperfect, but it seems to justify the belief that the disease was really yellow fever.

The highest medical authorities in Brazil agree that yellow fever was not endemic in the principal seaports of the empire prior to the year 1849, when it was introduced into the city of Bahia by the North American brig *Brazil*, which sailed from New Orleans, where yellow fever was prevailing, and touched at Havana. Two of the crew of this brig died of yellow fever during her voyage from the latter port to Bahia. Soon after her arrival the disease made its appearance among those who had communicated with the ship, and later on other vessels in the harbor. The first case occurred a few days after the arrival of this brig (November 3d). A part of her cargo is said to have consisted of little barrels of beef which had become putrid. From Bahia the disease was carried to Rio Janeiro, where during the epidemic season of 1850 it caused a mortality of 4,160.

According to Professor Barata, of the Faculty of Medicine of Rio Janeiro, yellow fever continued to prevail in Brazil until the year 1861, when it disappeared for eight years, to reappear in 1869–70, as the result of a fresh importation. The Italian ship *Creolla del Plata*, which had touched at St. Iago, where yellow fever was prevailing, is named as the vessel which introduced the disease on this occasion.

The mortality from the disease under consideration in the city of Rio from the time of its introduction in 1850 to the year 1886, is shown by the following table:

	Mortality		Mortality.
1850	4,160	1869	274
1851	455	1870	1,117
1852	1,943	1871	8
1853	853	1872	102
1854	21	1873	3,659
1855	0	1874	829
1856	0	1875	1,292
1857	1,425	1876	3,317
1858	800	1877	282
1859	500	1878	1,174
1860	1,249	1879	954
1861	247	1880	1,433
1862	12	1881	219
1863	0	1882	95
1864	0	1883	1,336
1865	0	1884	618
1866	0	1885	278
1867	0	1886	1,397
1868	0		

In 1855 yellow fever is said, by Hirsch, to have prevailed extensively in Brazil, although this was not an epidemic year in Rio Janeiro. The following year it extended along the Amazon far into the interior of the country. The years of greatest epidemic prevalence since that date have been 1859–60, 1862, 1869–70, 1872–73, 1875–77 (Hirsch).

From Brazilian ports the disease has occasionally been introduced into the cities at the mouth of the Rio de la Plata, and has there caused great loss of life. The first epidemic at *Montevideo* was in 1857, and it was again introduced into this city, from Pernambuco, in 1872. It prevailed in the city of *Buenos Ayres* in 1858 and in 1870.

Yellow fever is said to have been conveyed to the Pacific coast of South America by a party of German emigrants, who landed at Callao, *Peru*, in 1854. The disease spread from this port to the capital, and in the course of the next two or three years to the principal towns upon the Peruvian coast, where it continued to prevail up to the year 1869.

Chili, up to the present time, has remained exempt from the disease (Hirsch).

Upon the *West Coast of Africa* the headquarters of yellow fever is that portion of the coast which belongs to the province of *Sierra Leone*, and epidemics at other points upon the African coast have frequently been traced to this locality. It seems very doubtful, however, whether, as some authors suppose, this is really the original source of the disease. The French authors Bérenger-Feraud and Bourru both call attention to the fact that we have no account of the disease prior to the year 1778, although the African coast was discovered and colonized long before the discovery of the West Indies; and that, on the other hand, the early settlers in these islands suffered from a pestilential malady which very probably was yellow fever.

At *St. Louis* (Senegal) an epidemic occurred in 1778, and this is the first outbreak of the disease of which we have any reliable information in this portion of the world. The disease in this instance is said by Schotte to have been imported from *Sierra Leone*, where epidemics are recorded to have occurred during the past century in 1816, 1823, 1825, 1829–30, 1837–39, 1845–47, 1859, 1862, 1864, 1865–66, 1868, 1878 (?) (Hirsch). Frequent epidemics have also occurred at *Senegambia*, and the disease has prevailed upon the *Gold Coast* (1852, 1857, 1862), the *Congo Coast* (1816, 1860, 1862, 1865), at the *Cape Verde Islands* (1845, 1862, 1868), and the *Canary Islands* (1701, 1771, 1810, 1846, 1862).

In Europe the ravages of yellow fever have been restricted mainly to the Iberian peninsula. This is due, no doubt, to the frequent intercourse between Spain and Portugal and the West Indian ports, in which the disease is most prevalent, and to the fact that the summer temperature of these countries is favorable for the epidemic extension of the disease; whereas the more northern portions of Europe are practically outside of the yellow-fever zone.

The first epidemic in *Spain* occurred in the year 1700, at Cadiz. This city also suffered in 1730–31, 1733–34, 1764, 1780, 1800, 1804, 1810, 1819–21. The epidemics of 1800, 1810, and 1819 were not limited to the city of Cadiz, but the disease extended to the interior and caused a considerable loss of life in the provinces of Granada and Andalusia, and also in some of the towns of Murcia and Catalonia—especially in Barcelona, from which city the disease was conveyed to the island of Majorca during the last epidemic. No widespread epidemic has occurred in Spain since 1821, but local outbreaks, as a result of importation from the West Indies, have occurred in Gibraltar (1828), Barcelona (1870), and Madrid (1878).

The first epidemic at *Lisbon* was in 1723, a second was inaugurated in 1856, and during the following year developed into a devastating scourge which extended to the towns of Belem, Olivaes, and Almada.

In *Italy* yellow fever has only once effected a temporary lodgment—at Leghorn, in 1804, into which city it was imported from Spain.

Ships with yellow fever on board have occasionally arrived at English and French ports, but local conditions have apparently not been favorable to an extension of the disease, except to a limited extent at Brest, in 1856, at St. Nazaire, in 1861, and at Swansea (Wales), in 1864.

Bahama Islands.—Yellow fever prevailed as an epidemic at Nassau in 1861, 1862, 1863, and in 1869.

According to Hirsch, yellow fever prevailed, to a limited extent, at Halifax (latitude 44° 26′), in 1861, and at Quebec (latitude 46° 50′), in 1805.

Prevalence of Yellow Fever in the United States.—*New Hampshire.*—Portsmouth is the most northern point in the United States which has suffered an epidemic of yellow fever. In 1798, and again in 1802, during which year the disease was epidemic in New York and in Philadelphia, it was also epidemic in this city.

Massachusetts.—In 1693 an English expedition sailed from Boston for the purpose of taking from the French the island of Martinique. The expedition failed in its object and returned to Boston on June 17th, with yellow fever on board the vessels of the fleet. Hutchinson, in

his "History of Massachusetts Bay," says the mortality among the sailors had been 1,300, out of a total strength of 2,100, and that out of the same number of soldiers the loss was 1,800. He states that the disease spread from the fleet to the town, and that many families left town and resided in the country until the infection had ceased. This is the first authentic account of the occurrence of yellow fever within the present limits of the United States. In 1796 the disease prevailed to a limited extent in Boston and in Newburyport. In 1798 it prevailed as an epidemic in Boston, where the mortality was 200, and, in 1802, 60 fatal cases occurred in the same city. Some cases also occurred in the years 1800, 1819, and 1858.

Rhode Island.—The city of Providence was several times visited by yellow fever during the latter part of the eighteenth and the beginning of the last century —1794, 1795 (mortality 45), 1797 (mortality 45), 1800, 1805. The disease prevailed at Newport in 1798, and at Bristol in 1797.

Connecticut.—The disease prevailed at New London in 1795, and again in 1798, when the mortality was 81. Hirsch records the occurrence of the disease at New Haven in 1743, 1794, and 1805; at Middletown in 1820; at Chatham in 1796, and at Hartford in 1799.

New York.—Epidemics of greater or less extent have occurred in New York City and its immediate vicinity in 1693, 1702, 1743 (mortality 217), 1745, 1762, 1791, 1794, 1795 (mortality 730), 1798 (mortality 2,080), 1799 (mortality 76), 1800, 1801, 1803 (mortality 700), 1805 (mortality 340), 1809, 1819, 1822 (mortality 230), 1848, 1853, 1854, 1856, 1870 (mortality 49).

New Jersey.—Hirsch records the following local epidemics: Bridgetown, 1798, Chews, 1798, Woodbury, 1798, Perth Amboy, 1811.

Pennsylvania.—According to La Roche "the earliest onset of the disease occurred in 1699, when Philadelphia, then but seventeen years of age, was little more in point of extent than an ordinary country town." There are no medical accounts of this epidemic, but there is no doubt as to the nature of the disease, which caused a mortality of 220 in the new city, estimated to have contained less than four thousand inhabitants. The next epidemic in Philadelphia occurred in 1741, when the mortality was 250. Subsequent epidemics occurred in 1747, 1762, 1793 (mortality 4,041), 1794, 1797 (mortality 1,300), 1798 (mortality 3,500), 1799 (mortality 1,000), 1802 (mortality 307), 1803 (mortality 195), 1805 (mortality 400), 1819, 1820 (mortality 83), 1853 (mortality 128), 1870 (mortality 18).

Delaware.—In the epidemic of 1798 the city of Wilmington suffered a loss of 250.

Maryland.—Epidemics, for the most part of limited extent, have occurred in Baltimore in the years 1783, 1794, 1797, 1798, 1799, 1800, 1802, 1819, 1820, 1821, 1822, 1868, 1876.

Virginia.—At Norfolk epidemics are recorded as follows: 1737, 1741, 1794, 1795, 1797, 1799, 1800 (mortality 250), 1801, 1821, 1826, 1855 (mortality 1,807). An epidemic occurred at Petersburg in 1798, and at Alexandria in 1803. At Portsmouth the disease prevailed in 1852, 1854, and 1855 (mortality 1,000).

North Carolina.—Wilmington, 1796, 1800, 1821, 1862 (mortality 446); Newbern, 1799, 1864 (mortality 700); Beaufort, 1854, 1864 (mortality 68), 1871; Washington, 1800; Smithville, 1862.

South Carolina.—The first epidemic, of which we have any account, in Charleston, occurred in 1693; from this time epidemics have been numerous, and during the first half of the present century the physicians of Charleston generally considered the disease endemic in that city. That it was not seems to be demonstrated by the immunity enjoyed since 1871, an immunity which is probably due to the diminished commerce with infected ports in the West Indies, and to a more efficient quarantine service, since the fact has been recognized that the disease is not endemic.

The prevalence of yellow fever in Charleston, during the past century, is shown in the following table; recorded epidemics, prior to the year 1800, are as follows: 1693, 1699, 1700, 1703, 1728, 1732, 1734, 1739, 1745, 1748, 1753, 1755, 1761, 1762, 1768, 1770, 1792, 1794, 1795, 1796, 1797, 1798, 1799 (mortality 239). An epidemic occurred among the troops stationed at Hilton Head in 1862; Port Royal, 1877 (mortality 25).

Georgia.—At Savannah epidemics are recorded in the years 1800, 1807, 1808, 1817, 1819, 1820, 1827, 1852, 1853, 1854 (mortality 580), 1858, 1876; at St. Mary's in 1808 (mortality 84), and in 1854; at Augusta in 1839 and 1854; at Bainbridge in 1873; Brunswick, 1876, 1893.

MORTALITY FROM YELLOW FEVER IN CHARLESTON, S. C., PENSACOLA, FLA., MOBILE, ALA., NEW ORLEANS, LA., AND GALVESTON, TEXAS, DURING THE PAST CENTURY.

Year.	Charleston.	Pensacola.	Mobile.	New Orleans.	Galveston.	Year.	Charleston.	Pensacola.	Mobile.	New Orleans.	Galveston.
1800....	184			*		1841...		*	*	594	
1801						1842...	....		60	211	
1802	96	....		*		1843 ..	1	*	240	487	
1803....						1844...		*	*	148	400
1804....	118			*		1845...		*		2	
1805....	*					1846...		*		160	
1806						1847...		*	76	2,259	200
1807....	162					1848...		*	75	850	
1808						1849...	129		50	735	
1809				*		1850				102	
1810						1851...			*	16	
1811		*		*		1852...	310			415	
1812	*			*		1853...		*	115	7,950	536
1813						1854...	627	*	*	2,125	404
1814						1855...				2,670	
1815						1856...	211			74	
1816						1857...	13			199	
1817	272			814		1858...	717	*	*	3,889	34*
1818....		....	....	115		1859...					182
1819....	177	....	254	2,190		1860					
1820				*		1861					
1821....			*			1862...	*	*			
1822....	2	255	*	230		1863...	...	*			
1823				1		1864...	*			.....	259
1824....	235	....		108		1865					
1825....	2	*	*	49		1866...					*
1826	....	....		5		1867...		54	*	3,093	1,150
1827....	64	*	*	160		1868					
1828....	26	....	*	130		1869					
1829			159	255		1870.			*	585	
1830....	30	....		117		1871...	213			55	
1831....				2		1872...				40	
1832....				18		1873...		61	27	225	
1833....		....	....	210		1874...		118			
1834....	99			95		1875					
1835....	25			284		1876					
1836				5		1877					
1837			350	442		1878			90	600	
1838....	351	....		17		1879					
1839....	134	*	650	452	250	1880					
1840....	22			3		1887...		....	46	290	

Number of deaths not stated

Florida.—The principal seaport, Pensacola, has suffered frequent epidemics of yellow fever. Those which occurred during the past century are included in the table given above. Two epidemics are recorded as having occurred prior to the year 1800—1764 and 1765. At St. Augustine epidemics occurred in 1807, 1821, 1838, 1839, and 1841; at Key West in 1823, 1829, 1841, 1862, 1867, 1875, 1878, 1887, 1899; at Jacksonville in 1857, 1877, and 1888; at Fernandina in 1877 (mortality 498); at Tampa in 1839, 1853, 1871, 1887, 1888; at Miami, 1899.

Alabama.—The recorded epidemics in Mobile, prior to the year 1800, were in 1705, 1765, and 1766; subsequent epidemics are included in the table. Montgomery, 1853 (mortality 35), 1854 (mortality 45), 1855 (mortality 30), 1873 (mortality 102); Selma, 1853 (mortality 32); Florence, 1878.

Mississippi.—The town of Biloxi, on the gulf, has suffered from epidemics as follows: 1702, 1839, 1847, 1853, 1858, 1878, 1884, 1897; Pascagoula, 1847, 1853, 1875, 1878; Port Gibson, 1878; Shieldsborough, 1820, 1829, 1839; Port Adams, 1839, 1853; Grand Gulf, 1853; Natchez, on the Mississippi River, 1817, 1819 (mortality 180), 1823 (mortality 312), 1825 (mortality 150), 1827, 1829 (mortality 90), 1837 (mortality 280), 1839 (mortality 235), 1848, 1853, 1855, 1858; Vicksburg, 1839, 1841, 1847, 1853,

1855, 1858, 1871, 1873, 1878 (mortality 872); Jackson, 1853, 1854, 1878 (mortality 86), 1898. Holly Springs, 1878 (mortality 309); Greenville, 1878 (mortality 301); Grenada, 1878 (mortality 326); Canton, 1878 (mortality 180). Our record does not include numerous smaller places which suffered during the epidemic of 1878, Ocean Springs, 1897, Edwards, 1897.

Louisiana.—The first recorded epidemic in New Orleans was in the year 1769; other outbreaks prior to the last century were in 1791, 1793, 1794, 1795, 1796, 1797, 1799. The prevalence of the disease in this city subsequent to the year 1800 is given in the table. Baton Rouge, 1817, 1819, 1822, 1827, 1829, 1837, 1843, 1847, 1853, 1858, 1878 (mortality 193), 1898, 1899; Opelousas, 1837, 1839, 1842, 1853; St. Francisville, 1811, 1817, 1819, 1823, 1827, 1829, 1839, 1843, 1846, 1848, 1853; Shreveport, 1853, 1873 (mortality 759); Port Hudson, 1839, 1841, 1843, 1853, 1878; Thibodeaux, 1846, 1853, 1854, 1878; Washington, 1837, 1839, 1852, 1853, 1854, 1867; Morgan City, 1878 (mortality 109). Numerous smaller places during the epidemics of 1873 and of 1878; Franklin, 1898, Alexandria, 1898.

Texas.—The epidemics at Galveston are included in our table. Houston, 1839, 1844, 1847, 1848, 1853, 1854, 1858, 1859, 1864, 1867, 1870; Huntsville, 1867 (mortality 130); Hempstead, 1867 (mortality 151); Indianola, 1852, 1853, 1858, 1859, 1862, 1867 (mortality 80); La Grange, 1867 (mortality 200); Matagorda, 1862 (mortality 120); Navazota, 1867 (mortality 154); Rio Grande City, 1867 (mortality 150); Victoria, 1867 (mortality 200); Brenham, 1867 (mortality 120); Calvert, 1867 (mortality 250); Chapel Hill, 1867 (mortality 123); Columbia, 1867 (mortality 132); Brownsville, 1853, 1858, 1862, 1882; Laredo, 1903.

Tennessee.—Memphis, 1828, 1853, 1855, 1867, 1873 (mortality 1,244), 1878 (mortality 5,000), 1879 (mortality 485); Chattanooga, 1878 (mortality 135); Brownsville, 1878 (mortality 212); numerous smaller towns in 1878.

Arkansas.—Columbia, 1853; Fort Smith, 1823, Little Rock, 1873, Napoleon, 1853.

Kentucky.—Bowling Green, 1878; Hickman, 1878 (mortality 153); Louisville, 1878 (mortality 64).

Ohio.—Cincinnati, 1871, 1873, 1878 (mortality 17); Gallipolis, 1796, 1878 (mortality 18).

Illinois.—Cairo, 1873 (mortality 17), 1878 (mortality 51).

Missouri.—St. Louis, 1854, 1855, 1878 (mortality 16); New Design, 1797 (mortality 57).

Great Epidemics in the United States. 1793.—The city of Philadelphia, after enjoying an immunity from yellow fever for thirty-one years, suffered in 1793 a devastating epidemic. This epidemic, no doubt, resulted from importation, although a clear history of its introduction was not made out at the time, and the leading physicians of the city were inclined to attribute it to local origin, as a result of unsanitary conditions in connection with an unusually high temperature. La Roche says: "Dr. Rush and others laid great stress on a quantity of damaged coffee which was exposed, during the latter part of July, in a place (on a wharf and in the adjoining dock) and under circumstances which favored decomposition. Its smell was highly putrid and offensive, insomuch that the inhabitants of the houses in Water and Front streets, who were near to it, were obliged in the hottest weather to exclude it by shutting the doors and windows. Even persons who only walked along those streets complained of intolerable fetor, which, upon inquiry, was constantly traced to the putrid coffee."

As usual, the early cases were not recognized as yellow fever. Dr. Rush says: "The report of a malignant and fatal fever being in town spread in every direction, but it did not gain universal credit. Some of those physicians who had not seen patients in it denied that any such fever existed, and asserted (though its mortality was not denied) that it was nothing but the common annual remittent of the city. Many of the citizens joined the physicians in endeavoring to discredit the account I had given of this fever, and, for a while, it was treated with ridicule or contempt. Indignation in some instances was exerted against me." History has repeated itself, in this particular, many times in subsequent epidemics. The early cases, even in cities like New Orleans, where the physicians are well acquainted with the disease, are frequently called by some other name—"bilious fever," "pernicious fever," "malarial fever," etc.—and the physician who first ventures to name the prevailing disease "yellow fever" is treated with ridicule or with indignation.

It was not until the middle of August that a rapid succession of fatal cases convinced the physicians of the city that the fatal West Indian pestilence was again present in Philadelphia.

The presence of the disease was officially recognized on the 22d of August, when the mayor of the city gave orders for the cleaning of streets and general purification of the city. The disease continued to extend until early in October, when it reached its height. It did not cease entirely until about the 8th of November. During this short season of prevalence it caused an enormous mortality, distributed as follows: "August, 325; September, 1,442; October, 1,976; November, 118" (La Roche).

The population of the city at this time is estimated to have been a little more than 40,000, which gives a mortality of ten per cent. of the total population (total mortality 4,040). As more than 12,000 of the inhabitants fled from the city, the proportion of those who were attacked is very great. La Roche estimates the total number of cases at 11,000.

1797.—The epidemic of this year in the city of Philadelphia was less extended and less fatal. The whole number of deaths is estimated to have been about 1,300. The disease, as usual, commenced in the vicinity of the wharves (about the end of July). Unsanitary conditions, described by physicians who were witnesses of the epidemic, furnished the favorable local nidus for the exotic germ, which, according to a report of the College of Physicians of Philadelphia made in response to a request from the governor, was imported by two vessels, one from Havana and the other from Port au Prince. In this report the College of Physicians, contrary to the prevailing popular opinion and that of many prominent physicians, took the ground that the unsanitary local conditions were simply secondary or accessory causes, and recommended "a more stringent system of quarantine regulations, as the most effectual means of preventing the recurrence of the disease" (La Roche).

1798.—The epidemic of 1797 was followed the next year by a still greater one, which was not confined to the city of Philadelphia alone. The disease prevailed also in Boston (mortality 200), in Portsmouth, N. H. (mortality 100), in Newport, R. I. (mortality 2), in New London, Conn. (mortality 81), in New York (mortality 2,080), in Wilmington, Del. (mortality 250), and in Charleston, S. C. The mortality in Philadelphia was 3,645, distributed as follows: August, 626; September, 2,004; October, 943; November (from the 1st to the 5th), 72. The mortality, in proportion to the number of cases, in the city of Philadelphia, was enormous, being, according to La Roche, about as 1 to 1.27 of those attacked, or nearly eighty per cent. This is accounted for partly by the fact that the better classes of the community left the city as soon as possible after the outbreak of the disease, and the cases which occurred were consequently among the poorer classes, who inhabited the worst portions of the city. The prevailing ideas as to the treatment of fevers by depleting measures, were doubtless responsible to some extent for the excessive mortality. "The College of Physicians, faithful to the theory so long entertained by it in relation to the cause of the disease, assigned to the epidemic this year, as it had done to those of preceding seasons, a foreign origin" (La Roche).

1802.—An epidemic of smaller proportions prevailed in the year 1802, causing a mortality in Boston of 60, in Philadelphia of 307, in Wilmington of 86, in Charleston of 96. The disease also prevailed "extensively" in Baltimore, but no record of mortality is given. The preva

lence of the disease at the seaports mentioned, especially before the time of railroad communication, is not to be ascribed to an extension from one to the others, or to "an epidemic constitution of the atmosphere"; but it doubtless occurred, for the most part, as a result of independent importation from the usual source of the disease—the West Indies. Thus we find that in 1802, while Boston and Philadelphia suffered epidemics, New York, lying between the two infected points, was free from the disease (two cases only are reported).

1853.—Passing over the minor epidemics, for the most part limited to a single city, or by coincidence merely to two or more distant seaports, we come to the epidemic of 1853, which extended through portions of the States of Florida, Alabama, Louisiana, Mississippi, Arkansas, and Texas. The towns which suffered in *Florida* were Pensacola, Milton, and Tampa. In *Alabama*, Mobile (mortality 115), Cahawba, Citronelle, Demopolis, Fulton, Hollywood, Montgomery (mortality 35), Selma (mortality 82), were the principal towns visited by the scourge. In *Louisiana* the disease prevailed at New Orleans, with a mortality of 7,970, at Alexandria, Algiers, Bay St. Louis, Bayou Sara, Centreville, Clinton, Coultierville, Franklin, Opelousas, Pattersonville, Plaquemine, Shreveport, Thibodeaux, Trenton, Washington, and various smaller places. In *Mississippi*, Biloxi, Brandon, Clinton, Grand Gulf, Greenwood, Jackson, Natchez, Pascagoula, Pass Christian, Port Gibson, Washington, Woodville, Yazoo. In *Arkansas*, Columbia, Grand Lake, Napoleon. In *Texas*, Brownsville, Cypress City, Galveston, Hockley, Houston, Indianola, Liverpool, Richmond, Saluria.

1867.—The epidemic of this year was widely extended in the State of Texas. The first recognized case in New Orleans occurred on the 10th of June. The total mortality in this city was 3,093. Other towns visited in Louisiana were New Iberia and Opelousas. In *Texas* the first cases occurred at Galveston on the 26th of June, and the total mortality in this city was 1,150. Other places visited by the epidemic were Alleyton, Anderson, Austin, Bastrop, Brenham, Calvert (mortality 250), Chapel Hill (mortality 123), Corpus Christi, Danville, Goliad, Hempstead (mortality 151), Huntsville (mortality 130), Independence, Indianola (mortality 80), La Grange (mortality 200), Liberty, Millican, Navazota (mortality 154), Oldtown, Port Lavacca, Rio Grande City (mortality 150), Victoria (mortality 200).

1873.—Florida, Alabama, Mississippi, Louisiana, and Texas again suffered from an epidemic of yellow fever in the year 1873. At Pensacola, Fa., the first recorded cases occurred August 6th, and the total mortality was 61. In *Alabama* the disease appeared at Mobile on the 21st of August, and the total mortality was but 27; Montgomery suffered a loss of 102. In *Louisiana* the mortality in the city of New Orleans was only 225, although the epidemic had its origin in this city. It was imported by the Spanish bark *Valparaiso*, which sailed from Havana, June 15th, in ballast; arrived at the New Orleans quarantine station June 24th; was detained two days, and came to the city June 26th. The first case was the mate of this vessel, who was taken sick on board July 4th, while she was lying at the wharf. But for the sickness and death of the mate of the *Valparaiso*, the origin of this epidemic would have remained obscure, and the believers in the local origin of the disease would have had a strong case, for no other cases of the disease occurred on the *Valparaiso*. This is explained by the fact that the crew consisted of acclimated Spaniards, and the mate seems to have been the only susceptible person on board who could serve as a test of the infection of the vessel at her port of departure. From New Orleans the disease was carried to Memphis by the river steamer *Bee*. It caused a mortality in this city of 2,000. River steamers from New Orleans also carried the disease to Shreveport, La., where the mortality was 759. From Shreveport a refugee fled to the town of Calvert, Texas, where he was taken sick and died; an epidemic followed with a total mortality of 125. The disease was also introduced by refugees to the town of Marshall, Texas, where 36 deaths occurred. The epidemic of this year at Pensacola, Fla., was due to an independent importation, by the ship *Golden Dream*, and Montgomery, Ala., became infected through refugees from Pensacola.

1878.—The last extensive epidemic of yellow fever in the United States is that of 1878, which invaded 132 towns, and caused a mortality of 15,934, out of a total number of cases exceeding 74,000.

The origin of this epidemic was traced by the president of the Louisiana State Board of Health (Chopin) to the steamer *Emily B. Souder*, which arrived from Havana May 23d, and was moored at the foot of Calliope Street, New Orleans. Dr. Chopin says: "The first cases of yellow fever in New Orleans in 1878 were, undoubtedly, two of the officers of the above steamship, namely, Clarke, the purser, and Elliott, one of the engineers. Infected centres were developed in the vicinity of the houses in which these men were sick, but not until after an interval of several weeks, during which, probably owing to unfavorable conditions as to temperature, the 'germs' remained dormant, or at least multiplied so slowly as not to cause an outbreak of the disease."

Fortunately, this great epidemic has been carefully studied by a "Board of Experts, authorized by Congress," and we have a very complete history of its geographical extension, and of the deadly results which marked its course. The following data are from the report of this "Board of Experts."

Louisiana.—New Orleans mortality, 4,600; Allemands Station, 17; Baton Rouge, 193; Bayou Cypre, 7; Berwick City, 7; Buras Settlement, 3; Clinton, 15; Delhi, 34; Delta, 47; Donaldsonville, 71; Gretna, 53; Hammond, 5; Henderson, 18; Houma, 6; Jesuits Bend, 2; Labadieville, 24; La Fourche, 26; Lagonda and other plantations, 42; Morgan City, 100; Napoleonville, 8; Paincourtville, 15; Pattersonville, 47; Pilot Town, 17; Plaquemine, 125; Ponchatoula, 3; Port Eads, 13; Port Hudson, 11; St. Bernard Parish, 7; Tangipahoa, 50; Thibodeaux, 65; Teche Country plantations, 81.

Tennessee.—Bartlett, 9; Brownsville, 212; Chattanooga, 135; Colliersville, 56; Germantown, 35; Grand Junction, 74; La Grange, 37; Martin, 40; Mason, 24; Memphis, 5,000; Milan, 12; Moscow, 35; Nashville, 6 (all imported cases); Paris and suburbs, 23; Somerville, 57; White Station, 50; Williston, 11.

Alabama.—Decatur, 44; Florence, 50; Huntsville, 12; Leighton, 1; Mobile, 90; Stevenson, 6; Town Creek, 4; Tuscaloosa, 2; Tuscumbia, 31.

Mississippi.—Bay St. Louis, 82; Benton, 1; Biloxi, 45; Bolon, 34; Bovina, 7; Brown's plantations, 4; Canton, 180; Vicinity of Canton, 47; Dry Grove, 41; Friar's Point, 7; Gainsville, 2; Goodrich Landing, 12; Greenville, 301; Grenada and vicinity, 343; Horn Lake, 2; Handsboro, 16; Hernando, 80; Holly Springs, 309; Iuka, 3; Jackson, 86; Lake, 86; Lebanon, 10; Livingston, 10; McComb City, 21; Meridian, 91; Mississippi City, 15; Ocean Springs, 30; Osyka, 45; Pass Christian, 23; Pearlington, 24; Port Gibson, 115; Country about Port Gibson, 150; Refuge Landing, 11; Rocky Springs, 38. Scranton, 20; Stoneville, 15; Spring Hill, 6; Sulphur Springs, 5; Senatobia, 7; Terrene, 4; Vicksburg, 872; Vicinity of Vicksburg, 300; Water Valley, 64; Winona, 3; Winterville and vicinity, 26; Yazoo City, 9.

Kentucky.—Bowling Green, 19; Hickman, 153; Louisville, 64 (mostly refugees).

Ohio.—Cincinnati, 17 (refugees); Gallipolis, 18.

Illinois.—Cairo, 51.

Missouri.—St. Louis, 16 (Quarantine near St. Louis).

In 1897 yellow fever again prevailed quite extensively in several of the Southern States. The epidemic had its origin at Ocean Springs, Miss. Cases occurred in 42 localities, the total number reported having been 4,325, with a mortality of 484. In Mississippi the largest number of cases occurred at Biloxi, Edwards, Scranton, and Ocean Springs; in Alabama the principal centres of infection were Mobile, Montgomery, Whistler, and Flouraton; in Louisiana New Orleans furnished by far the greater number of cases (mortality 275).

Although, in the light of our present knowledge, it would appear that the prevention of yellow fever should be a comparatively easy matter, and it has in fact been eradicated from the city of Havana, which for years was one of its principal endemic foci, a recent (1893) epidemic within the limits of the United States, at Laredo, Texas, indicates that the history of yellow fever in this country may not yet be completed. There can be no doubt, however, that the extension of this disease could be absolutely arrested if all infected individuals could be protected from the attacks of mosquitoes of the species (S. fasciata) which serves as an intermediate host for the parasite, or if all the infected mosquitoes could be promptly destroyed.

George M. Sternberg.

YELLOW FEVER: SYMPTOMATOLOGY, MORBID ANATOMY, TREATMENT.—Definition.—Yellow fever is a communicable disease, traceable to populous centres of the littoral of the tropical Atlantic, and transmitted from man to man by the bite of the *Stegomyia* mosquito. The chief features of the disease are: (1) a fever of from two to seven days' duration, characterized by a sudden invasion and a fastigium of from one to four days' duration, followed by an irregular lysis which may be interrupted by a secondary exacerbation; (2) a steady fall of the pulse, commencing during the fastigium and leading to a remarkable slowing of the heart beat; (3) vomiting; (4) jaundice; (5) albuminuria; (6) a tendency to stasis of the circulation; and (7) to hemorrhages. The lesions consist of parenchymatous degenerations of the liver, kidney, and stomach.

General Description.—During the early hours of the morning the patient awakes with a slight rigor, and, on moving, experiences vertigo and numbness and heaviness of the lower extremities. This is followed by nausea, and in some instances by vomiting of the remains of the last meal; the temperature rises rapidly; frontal headache, rachialgia, and pains in the limbs develop, and the pulse becomes frequent. The face assumes an injected, turgid appearance; the eyes are red and moist. The patient looks like a person who has indulged in an alcoholic debauch. During the day the fever continues to rise and the patient complains further of discomfort, pain or burning in the epigastrium, with sensitiveness to pressure. The temperature rises to between 102° and 103° F. and the pulse to 100 or 110. After six or nine in the evening of the first day the temperature usually falls, remitting one or two degrees on the morning of the second day. After the initial elevation of the temperature the course of the disease may vary according to three different types: the descending or mild type, the continued type, and the remitting, complicated or secondary fever type. The vaso-motor erethism will begin to subside, together with the painful symptoms, after the diurnal elevation of temperature of the second day, and it is replaced either by the evidences of a gradual return to the normal, or by the signs of blood stasis with hemorrhages from the mucous membranes, or with the syndrome of a malignant icterus. The urine becomes albuminous on the second or third day of the disease. The mental attitude is usually one of alertness. Even when the patient is delirious the expression of the face is apt to be attentive, though the mind be utterly confused and the speech wild. In some cases there is somnolence. The pulse begins to fall on the second day, and continues to fall even though the temperature may rise. Recovery is usually rapid, and sequelæ are rare. Independently of the course of the temperature we may recognize certain types, such as the uncomplicated, the hemorrhagic, the icteric, the ataxic, and, as rarer forms, the anuric, the dystolic, and the fulminating. The various combinations of these, however, are of too frequent occurrence to give them any practical value. We shall find it of greater clinical import to study the symptoms in detail.

Duration.—The following table will give the duration of the fever in 275 carefully recorded cases:

Duration.	Recovered.	Died.	Duration.	Recovered.	Died.
Two days.....	2	0	Ten days.....	13	4
Three days.....	5	1	Eleven days....	3	1
Four days.....	7	4	Twelve days...	6	0
Five days.....	25	2	Thirteen days .	6	1
Six days.....	39	16	Fourteen days	2	1
Seven days....	56	13	Fifteen days...	1	1
Eight days.....	27	7	Twenty days :	0	1
Nine days.....	19	11	Twenty-three days...	1	0

From the above table it will be seen that the duration of the cases that end in recovery is, in the majority of instances, seven days; and that fatal cases are more apt to terminate on the sixth day. Cases of more than ten days' duration are comparatively rare.

Temperature.—In the classical descriptions of yellow fever, dating from the period before the thermometer came into general use, we find it stated that a remission, occurring about the third day of the disease, is a prominent feature of the thermic curve of yellow fever. Some authors speak of this disease as a fever of two paroxysms separated by the so-called period of calm. If we disregard the readings of the thermometer we frequently are impressed with the accuracy of this description. As the vascular erethism of the period of invasion subsides, there is a marked change in the appearance of the patient. In grave cases there is a tendency to stasis; at the same time internal hemorrhages may be setting in. Hence the extremities become cold. Especially about the wrists we observe coolness of the surface with or without moisture. But all this does not coincide necessarily with a fall of the internal temperature. In yellow fever, as in other diseases in which definite lesions of an acute character set in during the first week, oscillations of the temperature, remissions, secondary fevers occur with more or less frequency. We are, therefore, not surprised to find that temperature charts of plague, scarlet fever, variola, and measles, resemble very closely those of yellow fever. The tropical form of malaria, in

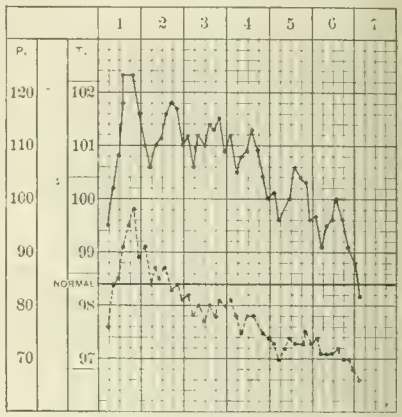

Fig. 5252.—Composite Chart of Eighty Cases of Yellow Fever, all Ending Favorably on the Seventh Day. Temperature, ——; pulse, ...

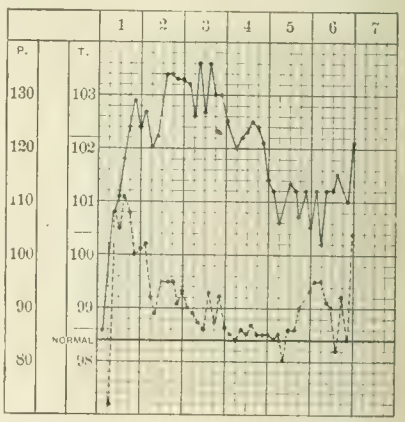

Fig. 5253.—Composite Chart of Twenty Cases of Yellow Fever, all Ending Fatally on the Sixth Day.

its primary manifestations, also frequently resembles the remitting type of yellow fever.

I have decided to present two composite charts of yellow fever. Such charts are usually of little value because the averages are obtained from cases that vary as to their intensity, their duration, and their termination. Butwith the large material at my disposal, I have been able to present two groups of the most common class of cases, namely, the cases terminating favorably on the seventh day, or morning of the eighth, and those terminating fatally on the sixth day (see Figs. 5252 and 5253).

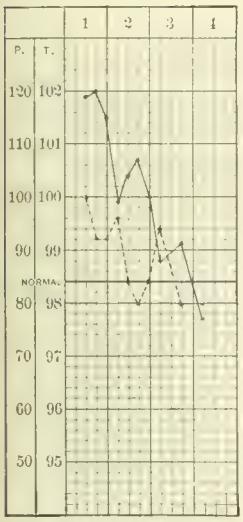

FIG. 5254.—Descending Type; Recovery.

As stated in the general description of the disease three types of thermic curve are found in yellow fever:

1st. *The Descending Type.*—It is usually mild. It is described by Finlay under the name of abortive type. It represents the inflammatory fever and the acclimating fever of creole physicians. The temperature reaches its acme on the evening of the first or second day, and descends in two, three, or four days through a down-grade series of oscillations. Occasionally such cases may end fatally on the third or fourth day without a secondary rise (see Figs. 5254 and 5255).

Remitting Type.—Usually severe. Many of the fatal cases present a secondary rise of the temperature which generally follows a depression caused by hemorrhage. The persistency of the hemorrhage may cause a second depression followed by a third rise of the temperature. Many cases of the remitting type end in recovery, and some may be quite mild (see Fig. 5256).

It will be observed in Fig. 5257 that the remission occurs during the first night of the disease. This case is one of the experimental cases inoculated by mosquitoes at Las Animas Hospital in Havana. This early remission is certainly not the remission referred to in the classical descriptions of the disease. Other observers have not had the opportunity given us by the experimental cases to study the development of the fever during the first twenty-four hours. Now, this early remission, heretofore undescribed, occurs in quite a number of cases, and is, to me, a more striking phenomenon than the later remission so much insisted upon by many authorities (see Fig. 5257).

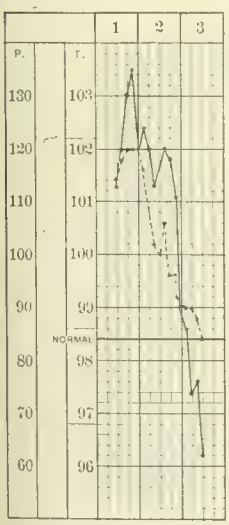

FIG. 5255. Descending Type; Fatal on the Third Day. Suppression of urine, uræmia on the second day. Black vomit early the third day.

Continued Type.—Usually fatal. The temperature need not be very high, but it is maintained at the same level for several days with very small oscillations. The black vomit will appear late in the disease, when the fall of the temperature is well established, showing the relation that exists between the two symptoms. These cases are apt to terminate with uræmic convulsions, the amount of urine being large and of low specific gravity. The patients are restless (see Fig. 5260).

The diurnal oscillations of the temperature vary considerably, conforming in general with the normal type; the minimum is reached about 6 A.M., and the maximum between 3 and 6 P.M. A rapid rise or fall may present itself at irregular hours, but a regular *typhus inversus* is rarely met with.

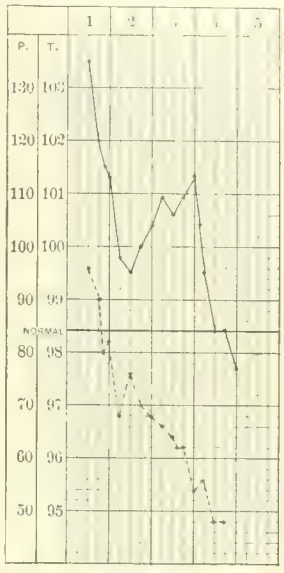

FIG. 5256.—Remitting Type; Recovery.

The Pulse. — In the stage of invasion, and during the first and, perhaps, the second day of the disease, the pulse is similar to that of other acute febrile diseases. It is large, bounding, and frequent in proportion to the elevation of the temperature. But during the second or third day the frequency of the pulse diminishes, and may continue to drop until very slow readings are reached at the time of the defervescence. The fall of the pulse does not follow upon a corresponding fall of the temperature. The body heat, in fact, may rise or may continue at the same level while the pulse is falling. This deviation from the usual correlation between the temperature and the pulse constitutes one of the most characteristic features of the disease. The temperature and pulse charts that have been selected for this paper illustrate the point in question. Even when the general trend of the pulse line does not conform with the type I am describing, it will be noticed that at some time in the course of the disease, be it only for a few hours, a falling pulse will coincide with a rising temperature. It is quite rare to find a chart of yellow fever in which at least an occasional manifestation of this phenomenon does not show itself.

The pulse on the first day will rise to about 110. In the descending type of temperature the pulse will rapidly fall and may reach 45 or 50 with the defervescence. If there be a secondary rise of the temperature the pulse may be but slightly, or not at all, affected by it. In fatal cases, however, the pulse will become frequent in the last stages of the disease, and it is quite common to find under these circumstances a gradual or sudden fall of the temperature with a progressive elevation of the pulse —a symptom of very grave import.

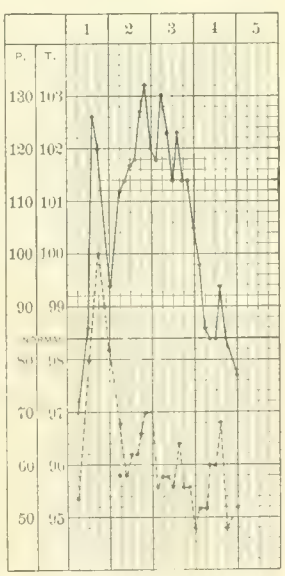

FIG. 5257.—Remitting Type; Recovery. Experimental case.

The relatively slow heart beat in complicated cases, during the secondary rise of the temperature, may be deceptive to the inexperienced. He who has watched with apprehension the steady increase in frequency of the pulse in grave cases of pneumonia, typhoid, or the eruptive fevers, can scarcely suspect the signs of approaching

dissolution in a patient whose pulse is beating regularly and with fair volume at the rate of 70 per minute. There will be, however, a diminution of the blood pressure in such cases, with some coldness of the extremities, a cyanotic hue about the lips or of the whole surface of the body, and a sighing respiration, that should arouse our fears.

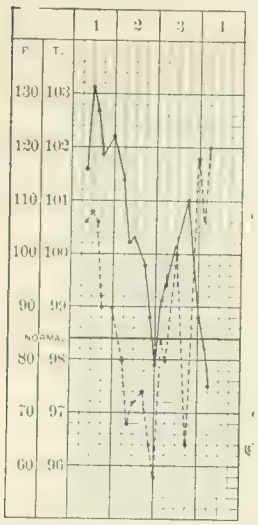

FIG. 5258.—Remitting Type; Fatal. Anuria, Jaundice.

The slow pulse may show considerable tension, specially in cases in which the icterus is well marked. The frequent pulse of the last stages in fatal cases does not differ from the preagonic pulse we find in other diseases.

The Facies.—The face is decidedly flushed, suffused with red of the same hue as that of scarlet fever. The eyes are injected and bright. There is a slight tumefaction of the lids and the lips. Even on the first day we may notice already in connection with this injection of the superficial capillaries a fleeting shade of yellow. This early manifestation of jaundice is undoubtedly the most characteristic feature of the facies of yellow fever. There is really no distinct jaundice. In the classical descriptions of the disease jaundice is not mentioned until the third day of the fever; but I hold that even at the earlier date we can detect a slight yellow tinge masked by the peripheral hyperæmia. Transient contractions of the capillaries will bring out this discoloration, for instance, in the imprints of the fingers when we pick up a fold of the skin, or in the conjunctivæ with the varying movements of the eyes. Often more distinctly at a distance than upon close inspection we notice a faint yellow glimmer pass over the eye. The same is true of the face, as may be seen when the facial muscles contract in speaking or smiling, and the redness transiently pales. Later in the disease, about the third day, these waves of color may become quite decided. The redness begins now, specially in severe cases, to assume a purplish hue; the jaundice becomes more pronounced, and the contrast between the two colors is sharper.

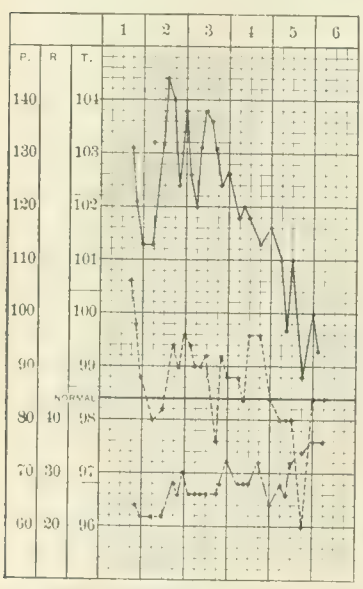

FIG. 5259. Remitting, Irregular Type; Fatal. Albumin in the urine on the morning of second day. Gastric hemorrhage begins with the drop of the temperature on the evening of the second day, and continues abundantly to the end. Urine scanty, loaded with albumin. T., ——; P., ...; R., — · — · —.

The features above described are, of course, more striking in the fair Northern races. It is only in connection with the darker races that we may accept the descriptive simile made by those who liken the color of the skin in yellow fever to that of mahogany.

The mental attitude and the subjective symptoms have their natural influence upon the facial expression. During the first day the eyes are frequently closed on account of the photophobia, and the expression of the face is that of pain from the cephalalgia and rachialgia. Later on, there may be somnolence, from which, however, the patient is easily aroused; but more frequently the expression is bright and alert, whether the mind be clear or not.

The mind is always clear in mild cases, and frequently also in the graver and fatal cases even to the last day.

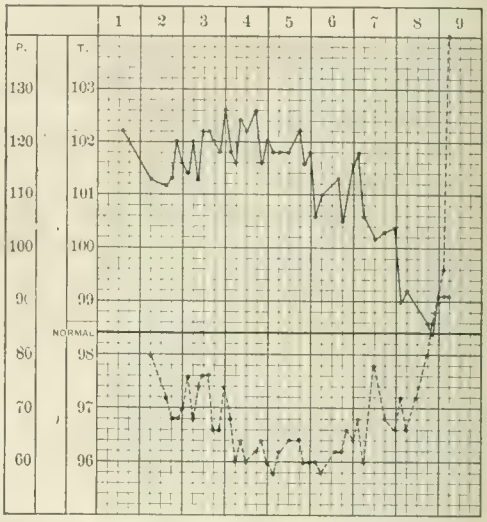

FIG. 5260.—Continued Type; Fatal. Black vomit begins at 7 P.M. on the seventh day, and is never profuse. Convulsions.

The excitement, the panic, that prevails in cities invaded by the epidemic, reflects upon the minds of the patients in the Southern States of the American Union. They are alert, watchful, suspicious as to the nature of their disease. They are apt to be nervous and excited. The Spaniard in Cuba who takes, or rather used to take, the disease as a matter of course is more calm or indifferent. All patients are apt to be rather talkative, and the dry mouth, the rather precipitate speech, reminiscent in character, are peculiar, and may be premonitory of a

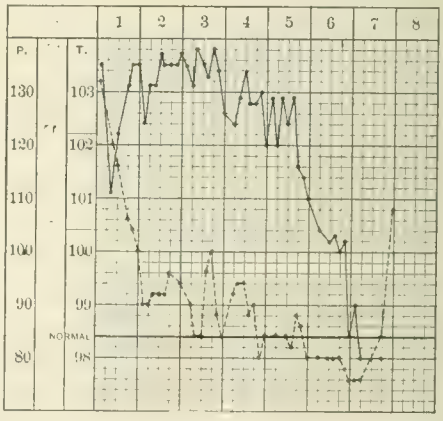

FIG. 5261.—Continued Type; Fatal. Black vomit once, at 2 P.M. of the sixth day. Delirium. Convulsions. Urine of the sixth day 1,180 c.c. with a specific gravity of 1.010. Albumin appears on the second day and is never abundant.

rather active delirium. If there be stupor it may be somnolent or wakeful, and accompanied with a staring expression. The delirium is talkative, and may be gay

or furious, generally dominated by some fixed idea: a notion that there is some urgent reason for the patient to leave his bed and quarters. His attempts to do so are, however, generally aimless, and limited to tossing about and sitting up in bed. It is very seldom that any restraint becomes necessary. Quite often there is, after the partial or complete loss of consciousness, a persistent and loud moaning which may be kept up during one or two days before death. Some cases of long duration present all the features of the typhoid state. Finally, we may have profound coma or convulsions.

Psychical disturbances, usually transient, may show themselves during the convalescence. I think they are less common than in typhoid fever and influenza.

Pains.—The supra- and intraorbital pains are perhaps the most distressing and persistent. They often disappear after the invasion, to recur with secondary elevations of the temperature or as a uræmic manifestation. The pains in the back and limbs may also be very distressing, and may even cause the patient to cry out in anguish. I have met with such severe aching only in cases of smallpox. In light attacks, however, the pains may cause little or no distress. Occasionally there are marked hyperæsthesia of the skin and deep-seated tenderness of the muscles. During convalescence it is not very rare to meet with painful neuritis, specially of the lower extremities. It usually affects one leg more than the other, and is accompanied with paræsthesia and very slight paresis. In my experience there has been only one case of serious peripheral palsy with atrophy, lasting several months and ending in recovery. Articular pains are rare. They are probably due to secondary infections, and may be accompanied with slight swelling of the joint.

The Skin.—After the first or second day the skin is apt to be moist, or at least the perspiration can be readily brought out by warm covering, or hot drinks, or other diaphoretics. Even during the first two or three days a slight moisture may alternate with a dry burning skin. When there is a marked remission it may be accompanied with a profuse perspiration, whether the defervescence be final or not; so that an active skin cannot be looked upon as a favorable sign or the indication of a critical discharge. A moist, clammy, cyanotic skin is frequently met with in grave cases after the third or fourth day of the disease.

Odor.—These perspiring patients are frequently malodorous, especially when, as is not rarely the case, a forced diaphoretic treatment is insisted upon; but I have never been able to detect in yellow fever an odor that may be called specific.

Rash; Eruptions.—The redness of the skin, previously described, is usually most marked about the face and neck, but it may be circumscribed in patches like an irregular scarlatina, an erythema, or the eruption of dengue. Rarely, faint irregular blotches may be seen, resembling the initial rash of variola. Occasionally we meet with sudamina, and very rarely with discrete pustular eruptions. An erythema and excoriations of the scrotum have been described by some authors, but I believe them to be exceptional and connected with chronic affections of the skin in these regions.

Gangrene is an extremely rare complication of the later stages, or of the period of convalescence, of yellow fever. I have seen once gangrene of one leg as the result of a secondary endocarditis. Other forms of localized gangrene about the scrotum or about the mouth are probably connected with neglect in the management of the disease.

Suppuration is, I believe, less frequently met with in yellow fever than in any other infectious disease. Abscess of the liver, suppuration of the parotids, deep-seated muscular abscesses are mentioned in the literature, but I have never encountered such complications. It is probable, therefore, that the secondary infections, evidences of which appear to exist in the clinical history, are not caused by pyogenic micro-organisms. I have suggested that the Shiga bacillus, a member of the hemorrhagic group, may be responsible for the secondary infections.

Digestive Apparatus.—The lips may be red and slightly swollen. In the later stages of the disease they will be purplish in severe cases. Herpes labialis is not common. The gums, specially of the upper jaw, are usually somewhat swollen on the second or third day, and covered with a thin creamy coating which is apt to form a faint line upon the gum at some little distance from the neck of the tooth. Later on, the gums are almost always spongy, and inclined to bleed, either spontaneously or upon pressure.

The tongue presents no symptom of interest. It carries no special coating, and may be somewhat pointed and red about the edges. In hemorrhagic cases when the hæmophilic symptoms have shown themselves, the tongue is usually pointed, smooth, crimson, and moist; it may also present bleeding cracks upon the surface. At the same time the mucous membrane of the mouth and fauces will show a similar appearance.

Exceptionally the parotids are the seat of swelling in the initial stage of the disease. This is probably due to inflammatory œdema. The tumor is rather soft, and disappears before the end of the attack. I have never seen suppuration of these glands.

The Stomach.—Vomiting is by no means a constant symptom in yellow fever. As an initial symptom I believe it to be more common in variola and scarlatina. At this stage it is merely vomiting of portions of food still remaining in the stomach, and occurs but once, at the beginning of the attack. Persistent vomiting is a grave symptom; it may continue upon the initial manifestation, or, more frequently, it will begin on the second or third day. As a rule the vomiting will cease if the stomach be given absolute rest. The vomitus, if we exclude the initial emptying of the stomach, consists of a watery, somewhat opalescent material, containing variable quantities of mucus. Later in the course of the disease, if the vomiting should persist, it is apt to become hemorrhagic, as will be shown at first by the presence of minute brownish and black specks floating on the surface; then the specks increase in size and number, the liquid becomes darker, until we have the characteristic black vomit. In these severe cases, in the intervals—which may be long or short—between the acts of vomiting, the patient is usually tormented with constant nausea, or distress and burning at the epigastrium, or hiccough, and a sensation of rawness and burning along the œsophagus. Black vomit may be absent in severe and even fatal cases, but then the black fluid will almost certainly be found in the stomach at the autopsy.

Vomiting is frequently absent in mild cases unless provoked by medication; but epigastric tenderness upon pressure is rarely absent. We should note also epigastric pulsation as a frequent symptom.

The bowels are usually sluggish, but amenable to the action of cathartics. The stools are often normal; they are not clay-colored, but in hemorrhagic cases they are frequently dark, tarry, or bloody.

The Liver.—Jaundice.—The liver is not appreciably enlarged, but may be sensitive to pressure. The lesions that will be described in connection with this organ are, in part, sufficient to account for the jaundice on the generally accepted theory of a hepatogenous origin. The areas of swollen, necrotic, dislocated hepatic cells; the round-cell infiltration of the perilobular zone could evidently, and no doubt they do, give rise to obstructions in the canalicular system; but the liver cells do not seem to be very active in the transformation of blood into bile pigment; they do not themselves become overcharged with pigment as is usually the case in obstructive jaundice. In yellow fever the liver seems to be comparatively less jaundiced than are other organs and tissues. The excess of hæmoglobin in the blood would lend support to the opinion that we have here to do with a form of polychromic icterus, but the liver cells are so generally disorganized that one cannot readily accept their ability to elaborate and transform the excess of blood pigment.

Here, more so than in connection with any other disease, it seems to me that the clinician should be loath to give up altogether argument in favor of a hæmatogenous jaundice, or at least in support of the view that something else than bilirubin may give rise to the yellow discoloration.

Jaundice is seldom, if ever, absent in yellow fever. It may be very slight, perhaps disputed, in some mild cases. Also in the rapidly fatal cases it may not show itself until after death. The dead body is always yellow in this disease.

When speaking of the facies I have mentioned a slight yellow discoloration among the initial symptoms of the disease. I believe it may be observed sometimes before the actual invasion. This symptom is first noticeable in the sclerotics. Now it is here also that the distinct jaundice of the third or fourth day of the disease first shows itself. It may be limited to this region, or more frequently it extends, growing in depth, and invading the regions that were most intensely flushed during the initial hyperæmia, until the whole body may become saffron-colored. Usually the jaundice is not so intense as it is in cases of obstructive icterus, or in Weil's disease; the color does not tend to assume a greenish hue, but is rather modified by the concomitant, more or less dusky, red, or purplish hyperæmia. The jaundice increases during two, three, or four days, and then disappears rather rapidly, leaving usually no traces by the end of convalescence. The intensity of the jaundice is not of itself a symptom of grave import, especially if it be not accompanied by a marked hemorrhagic tendency; but the early manifestation of the symptom, a well-developed jaundice, for instance, on the second day, indicates a fatal termination.

The Urine.—Quantity and Specific Gravity.—The daily averages for cases of seven days' duration, all ending in recovery, are given in the following table:

Day.	Quantity. C.c.	Specific gravity.	Day.	Quantity. C.c.	Specific gravity.
First	820	1.020	Fourth	1,206	1.018
Second	991	1.017	Fifth	826	1.019
Third	1,084	1.018	Sixth	850	1.017

The daily averages for fatal cases of six or seven days' duration are represented in the following table:

Day.	Quantity. C.c.	Specific gravity.	Day.	Quantity. C.c.	Specific gravity.
First	775	1.022	Fourth	1,220	1.013
Second	809	1.018	Fifth	892	1.013
Third	1,113	1.015			

In the last two days the urine is frequently lost. The specific gravity is usually low, and the amount is reduced even to absolute anuria; though the cases are by no means rare in which the quantity and density of the urine are not seriously disturbed.

In all cases, mild or grave, the amounts of urea and of the chlorides gradually diminish during the fever.

Albumin.—The presence of albumin in the urine constitutes one of the chief characteristics of this disease. If we divide the cases of about one week's duration in two groups, those ending in recovery, and those ending fatally, we shall obtain the following instructive table:

Albumin appears	Recovered, per cent.	Fatal. per cent.
On the first day in	2	33
On the second day in	44	33
On the third day in	29	33
On the fourth day in	14	
On the fifth day in	8	
On the seventh day in	2	

In the large series of cases that constitute the basis of this article, albumin was found in all. It is true that some, that were perhaps cases of yellow fever, may have been excluded precisely because of the absence of this symptom; but, if accepted, they would have been at best but doubtful cases. In none of the infectious diseases is albuminuria so frequent a symptom. I must admit, however, that the careful examination made of the urine in all kinds of fevers has shown that this symptom is met with—more frequently than is generally believed—in influenza, typhoid, and malaria. In these diseases, however, unless the infection be severe, the amount of albumin is less, or the date of its appearance later, than in yellow fever.

Urobilin is frequently found in the urine, and bile pigments in the cases in which jaundice is a prominent symptom. An abundance of the latter is looked upon by some as a favorable sign. Azevedo and Couto report that they often obtain crystals of leucin.

Hæmaturia is rare, and hæmoglobinuria I have never met with in uncomplicated cases.

Albertini has shown, and I have confirmed, that the diazo reaction is not obtained in yellow fever. Its presence may be looked upon as very strong evidence against this disease.

Casts are found in all but the very mild cases of yellow fever. They may be hyaline, granular, or epithelial. Sometimes they are found in great numbers, and one cannot help being amazed at the rapidity of their disappearance, together with the albumin, during the convalescence, or even before the fever has entirely subsided. A chronic form of parenchymatous nephritis, following upon yellow fever, is to be counted among the rarest of sequelæ.

Retention of urine is not rare, but in my experience complete suppression is an uncommon and almost always a fatal complication.

Respiration.—The breathing is not accelerated except moderately during the last twenty-four hours in fatal cases. Frequent sighing and hiccough are rarely absent in the grave cases.

The Blood.—The maintenance of a high percentage of hæmoglobin during the first three or four days of the disease was first discovered by Finlay. Albertini has made a clinical application of this fact, and we have found in a large number of cases values ranging between 90 and 105. The specific gravity of the blood is not correspondingly high. It varies, in fact, between 1,040 and 1,060. In 32 cases of yellow fever examined with this point in view, the percentage of hæmoglobin has been found below 90 in 3; 70, 75, and 82 respectively. In other diseases, such as typhoid and especially malaria, the readings are almost invariably low. We consider this sign to be of distinct diagnostic value.

The number of red blood cells is not diminished. This fact, first observed by Finlay and Delgado, has been more recently confirmed by myself and by Azevedo and Couto. The increase in the number of erythrocytes and in the amount of hæmoglobin may persist until the fifth day of the disease. The red cells show no change morphologically or in their color reaction. The number of blood plaquettes is increased.

Leucocytes.—In yellow fever we have hypoleucocytosis without any characteristic variation from the normal relations of the several kinds of leucocytes. The hypoleucocytosis gradually disappears during convalescence, and is followed by some augmentation of the number. There may be hyperleucocytosis during the preagonic period.

The relative proportion of the different kinds of leucocytes I have found to vary as follows: Polymorphonuclear from 60.50 to 79.50 per cent.; lymphocytes from 14.10 to 36.40 per cent; transition forms from 1.50 to 3 per cent.; large mononuclear from 1.78 to 9.50 per cent.

There is usually some increase of the mononuclears, but the readings are not so high as in malaria. The difference, as suggested by Gray, may be given some weight in the diagnosis, in the case of this disease. Eosinophiles are seldom found.

Hemorrhages.—Out of 277 carefully recorded cases, 122 presented hemorrhage as a noticeable symptom. Probably among the remaining 155 there were many with spongy gums that could be made to bleed slightly upon pressure. Of the non-hemorrhagic cases 148 patients recovered and 7 died; of the hemorrhagic 66 recovered and 56 died. The fatal cases had, with few exceptions, gastrorrhagia; most of them had at the same time other forms of hemorrhage. Of the patients that recovered 27 had black vomit. In most of these, however, the symptom was not pronounced; that is, the vomitus contained only more or less numerous specks of altered blood.

The character of the black vomit varies from the fluid just described, or one containing brownish flakes or striæ of a bright red color, to a black syrupy fluid. The amount varies considerably. Sometimes large quantities are repeatedly ejected with force to a considerable distance. In fifty two per cent. of the cases the first manifestations of black vomit present themselves about the fourth and fifth days. I have seen it as early as the second and as late as the eleventh day. There can be no doubt as to the nature of the dark fluid under consideration. The microscopic, chemical, and spectroscopic investigations show the presence of variable quantities of altered blood.

Bleeding of the gums and nosebleed are the most common forms of hemorrhage in yellow fever. Black vomit follows in frequency; but we should not forget that it is not always an evidence of gastrorrhagia, since the blood may have been swallowed from the mouth or nasal cavities. Melæna frequently occurs as a result of the hemorrhages above described, or from enterorrhagia.

Bleeding from the uterus and rectum, petechiæ, cutaneous hemorrhages are all quite frequent. Minute hemorrhages and more or less extensive ecchymoses are found in the internal organs post mortem.

As an explanation of these hemorrhages I have suggested the possibility of secondary infections with bacteria of the hemorrhagic group. I have once had the opportunity of testing the blood serum of a hemorrhagic case with a culture of the Shiga bacillus, and I found a positive agglutination with dilutions of 1 to 50. It is well known that the blood of yellow-fever patients will agglutinate at times the Zanarelli bacillus, and that the latter may be found in the tissues.

The hemorrhages usually occur with a falling temperature, and it does not seem quite clear that the fall is a consequence of the loss of blood. I rather incline to the view that both phenomena have a common cause.

Complications.—If we exclude the accidents that may occur in the course of the disease, and that have been already described, we may say that complications are quite rare. Pulmonary and cardiac inflammations are very infrequent. The authors of the excellent monograph in Nothnagel's "Specielle Pathologie," Azevedo and Couto, believe that endocarditis is a common complication, but such has not been my experience, nor that of American and Cuban observers.

Malaria is not a very rare complication. Its symptoms usually remain in abeyance for three or four days, and then resume their periodic character. The complication is a serious one, but by no means necessarily fatal.

Relapses.—Relapses are very rare. Accidents may occur in the course of a slow defervescence, giving rise to renewed fever; but a second attack, interrupting the course of convalescence, I have seen but once in carefully observed cases. I also have the records of a second attack occurring six weeks after complete recovery from the first. Both attacks were severe.

Termination.—The return to health is usually rapid. In the second week the patient clamors for food, and is anxious to resume his avocations. In severe cases the favorable result may be delayed by prostration, anæmia, impaired digestion with or without jaundice, paresis of the extremities, neuritis. Death results, in the majority of cases, apparently from intoxication affecting the nerve centres and from hemorrhage. Ataxic symptoms, delirium, convulsions, coma, crowd one another in the last hours of fatal cases of short duration. Other cases, usually with intense jaundice, have a less violent end, and die in an adynamic condition by asthenia.

Diagnosis.—The diagnosis rests mainly upon the four chief symptoms: the facies, the pulse and temperature, the albuminuria, and the tendency to hemorrhages.

In certain diseases, usually benign, such as influenza and dengue, that may be confounded with mild cases of yellow fever, the diagnosis is at times difficult. At the beginning of an epidemic the examination of several patients may be necessary.

In influenza we should expect to find the catarrhal symptoms, the peculiar appearance of the buccal mucous membrane and the tongue, the greater remissions of the fever, the pulmonary complications, the presence of the influenza bacillus. In yellow fever, on the other hand, we should find jaundice and albuminuria much more frequently than in influenza of the mild type that we are here concerned with; and then, besides, in yellow fever there is the peculiar pulse line.

In dengue we would rely upon the eruption and the articular and muscular pains, and upon the absence of jaundice and albuminuria.

With respect to graver forms of yellow fever it may be difficult to determine whether we are dealing with this disease or with typhoid, malaria, and malignant forms of jaundice, or, more rarely, with plague and relapsing fever.

Typhoid Fever.—Each one of the two diseases—yellow fever and typhoid fever—has its special facies. During the first week, when the mistake is likely to be made, the tongue in typhoid is heavily coated. The temperature is more regular, and the pulse frequency does not decrease. I need not mention other symptoms generally found in typhoid; but our opinion will be guided by the following facts: In typhoid our patient has probably been sick with fever two or three days; he is likely to have a temperature of 103° F. or thereabout. The following day he will have the same temperature. Now in yellow fever this would mean a quite severe form of the disease, and the patient ought to have a well-marked albuminuria. In typhoid he will have but little or no albumin. This may appear as a matter of little importance, a mere difference in degree, but it is not so. The pronounced albuminuria of severe cases of yellow fever is a very striking symptom, quite distinct from mere febrile albuminuria. The albumin may increase in typhoid, but a case of yellow fever with the temperature of a typhoid patient, kept up for several days, would be in a very grave state, and would show all the alarming and peculiar symptoms of the former disease. Besides, in typhoid we should have the diazo reaction in the urine, and a low percentage of hæmoglobin in the blood. At the time when the Widal reaction is obtainable the case is not likely to be mistaken for one of yellow fever.

Malaria.—The plasmodium in the blood in malaria, and the albuminuria of yellow fever are the main distinctive features. A great deal has been written about a certain form of malaria as likely to be confounded with yellow fever; I refer to the bilious remittent fever. I suspect that this name was generally given to the yellow fever of the natives of the yellow-fever zone who were supposed to enjoy immunity against this disease, or else it is a form of malaria that has disappeared from our malarial regions.

The real difficulty in diagnosis is encountered in connection with cases of æstivo-autumnal fever during the first days of the attack, and with cases of yellow fever in the first stage of the disease. It is precisely the absence of the so-called bilious symptoms at this time in the latter disease that renders the diagnosis difficult. We may have to wait for their appearance, as they are sure to come in a case of yellow fever having the high temperature and the stormy onset of the tropical form of malaria in an unacclimated person. The same may be said of the albuminuria; it will be a striking symptom of such a case, whereas in malaria, if present at all, it will be no more than an ordinary febrile manifestation. In

this disease the tongue will be flat, flabby, and coated; the liver and spleen will be enlarged; the hæmoglobin percentage will be about seventy or lower; the temperature is likely at some time to fall precipitously without any hemorrhagic symptoms; the pulse is sure to rise with the following access of fever; the malarial parasites will be found in the blood. We should remember also that a yellow-fever patient with the high temperatures that are likely to prevail in malaria, is a very sick man, whereas the malarial patient is less seriously affected.

In hæmoglobinuric fever the black water itself is very strong evidence against yellow fever, especially if we can prove the absence of red blood cells in the urine. The attack usually comes on after repeated paroxysms of intermittent fever with a severe chill, and the hæmoglobinuria and the jaundice, the enlargement and tenderness of the liver and spleen, with anæmia and low per centages of hæmoglobin in the blood, are prominent features from the start.

Malignant Jaundice.—Writers who were not familiar with yellow fever have supposed that there must be a marked resemblance between these affections, but this is not true. In acute yellow atrophy we have the following distinctive features: frequency of the disease in connection with pregnancy, prodromal gastro-hepatic disturbances, early development, and progressive character of the jaundice, absence of the sudden onset with fever and congestive symptoms, diminution in the size of the liver, change in the color of the fæces, presence of leucin and tyrosin in the urine, marked diminution of the amount of urea, great prostration, pallor, low percentage of hæmoglobin, and slight œdema.

In Weil's disease the history of the onset corresponds with that of yellow fever, but the gastro-hepatic symptoms are more pronounced from the beginning. The jaundice is more intense and presents a more greenish tint. There is a tendency to diarrhœa; the fæces are often clay-colored. The liver and spleen are large and tender. The muscular masses are sensitive to pressure. The hemorrhages, when present, are a later manifestation than in yellow fever. The duration of the disease is longer, its course being frequently marked by two distinct paroxysms. The patient falls very soon into a typhoid state, and finally the urine, according to some authorities, is apt to contain the Proteus flavescens.

Prognosis.—Attention has already been given to the prognostic significance of the several symptoms; hence it is not necessary to dwell extensively upon this subject. We may summarize the unfavorable prognostic signs as follows: maintenance of the temperature at a high level for several days; high temperatures coinciding with the appearance of the jaundice and hemorrhages; persistent vomiting after the initial emptying of the stomach; noticeable falls of the temperature after vomiting, with subsequent elevation; marked reduction of the arterial blood pressure; early development of pronounced jaundice, albuminuria, or gastric hemorrhage; loss of consciousness with active delirium or with a staring expression; profound coma; suppression of urine.

The mortality from yellow fever varies in the different epidemics. The series of 277 cases treated at Las Animas Hospital in Havana, which have been specially analyzed in this paper, gave a mortality of 22.7 per cent.

I have myself seen the range of mortality vary, in different epidemics, between 4 and 36 per cent. Among soldiers confined in barracks the mortality is said to have been as high as 92 per cent. It is low among children and very low in the full-blooded negro. I have not been able to find any decided differences in the mortality of the whites from the various nations. Reports to the contrary are, in my opinion, to be explained by accidental conditions affecting at the time one race more than another. The natives of one country, for instance, will be better looked after; they will come in for treatment earlier than others. At Las Animas Hospital the mortality among those who were admitted within the first forty-eight hours of the disease was 17.7 per cent., while among those who were admitted later it rose to 32.3 per cent. Now, the first were mostly Americans; the second were Spaniards, Italians, etc.

Before concluding this description of yellow fever I wish to state that though I have made special use of the material at my disposal, which is derived from the study of cases in Havana during 1900 and 1901, my knowledge of the disease is based upon the study of many epidemics observed in the United States, in Cuba, and in Mexico. I mention this because I wish to declare that I have found the disease everywhere and at all times to be always the same. The number of mild cases will be greater at one time than at others. There may be a difference in intensity; but, aside from this, I have never been able to discover characteristic features that would distinguish one epidemic from another.

Morbid Anatomy.*—External appearance of the body. The cadaver of yellow-fever patients presents a characteristic coloration. The shade of yellow is variable up to a deep saffron color. This is not uniformly distributed as in other forms of jaundice, but rather appears with greater intensity in the depending portions of the body. At the same time we find extensive areas of cadaveric lividity due to hypostasis. The face appears livid and turgid. From the mouth and nostrils we generally find oozing a dark fluid, or dark crusts or coagula are found about these orifices. The conjunctivæ are yellow and often ecchymotic.

The Heart.—This organ is not as a rule seriously affected in yellow fever. This opinion does not conform with that of Soudré and Couto as expressed in Nothnagel's "System of Medicine." The size and weight of the organ are normal. The consistence is generally firm, with few exceptions. The external aspect indicates in some cases a slight increase of the subpericardial fat, specially toward the base, and along the transverse and longitudinal furrows. This is not an evidence of degeneration since the underlying muscular tissue is generally found to be normal. On the surface we may find a few ecchymotic spots, but they are not more numerous than those found elsewhere. Soudré and Couto describe in one case a hemorrhagic focus about the size of an almond, involving the whole thickness of the left ventricular wall. On opening the heart the muscle appears somewhat paler than normal, and the thickness of the ventricular wall is normal, or may be slightly increased. This is described as constant by Couto and Soudré. The left auricle and the right side present nothing abnormal. Some post-mortem clots are generally found in the cavities. The endocardium presents to the naked eye, in some cases, a yellowish discoloration, more marked toward the tendinous extremities of the papillary muscles. Ecchymotic points may be seen generally near the large vessels. These are not constant changes. The valves may be slightly thickened toward the borders, but usually they are normal. The valvular thickening and vegetative endocardial lesions described by Couto and Soudré as constant, we have not been able to find.

Histology.—Alterations of the muscular fibre occur only in rare cases. The striation, which is never as distinct in the cardiac as in the voluntary muscles, shows quite clearly in most of our preparations as soon as we apply the sufficient amplification. The continuity of the fibre is not altered, and it is well known that in the degenerated heart this is easily broken. The nuclei take the stains readily, and do not present the deformities and elongations that are found in other infections. The interstitial connective tissue is not increased or proliferated. The vessels show no alterations. Occasionally we find small extravasations near the endo- or pericardium. The subpericardial fat appears to be somewhat increased. This probably explains the augmentation in the size of the organ. Rarely we have met with alterations in the muscular fibre. These are by no means uniform. More or less granular cells are found among perfectly normal ones. The former are slightly vacuolated, and their stri-

* This section has been written by Drs. Juan Guiteras and A. A. Abalil.—Editor.

ations may be completely lost. The nuclei will be found to take the stains, and to show no profound alterations. The fatty degeneration, described by others, we find to be exceptional. Nowhere have we found evidences of acute endocarditis. In one case we found a minute accumulation of round cells, separating muscular fibres which were perfectly normal.

The pleura and lungs present no lesions that are characteristic of yellow fever.

The Spleen.—Its size is usually not altered. On section the pulp presents a dark wine color, with reddish areas. The Malpighian corpuscles are not prominent. The consistence of the organ is somewhat diminished. Histologically we find the organ but slightly affected. The Malpighian bodies show neither proliferative nor degenerative lesions, but the connective-tissue stroma appears to be slightly increased. The parenchyma of the organ is congested. The small veins are particularly distended. In some cases we met with hemorrhagic foci. There is no increase in the amount of pigment contained in the spleen. Some authors describe cloudy swelling limited to small areas of the parenchyma. This we have not been able to confirm, nor have we found any appreciable change in the vascular walls.

The Kidneys.—By the naked eye we discover profound lesions that appear to be constant. The size is more or less increased. The color is generally yellowish-red. Upon section the color appears reddish-yellow or grayish. The vessels are dilated and the blood flows freely. The medullary zone contrasts with the cortical through the normal or somewhat cyanotic hue of the former. The capsule peels easily, and the surface appears reddish-yellow with vascular arborizations.

Morbid Histology.—Two kinds of lesions are found in our preparations: one is constant and the other variable. The glomeruli, though sometimes normal, present in most instances evident lesions. At times the capsule is thickened through proliferation of its cells, but it is more frequently normal, except that the epithelium, parietal or visceral, is more or less degenerated. The cavity is generally filled with an exudate of variable character. It may be granular, containing exfoliated cells, or it may present minute fatty areas or evidences of hyaline degeneration. The exudate takes a rose color with the hæmatoxylin-eosin stain, or gives the reactions of hyaline matter. The capsular degeneration does not appear to be constant; nor is it necessarily fatty, even in cases in which the fatty change is quite apparent in other portions of the kidney. The glomerule is retracted and small in proportion to the amount of exudate, and it rarely shows evidences of cloudy swelling. In our experience the more constant lesions are found in the convoluted tubules. Their lumen may be dilated, and contains granular matter from the disintegration of cells and from the coagulation of albumin. Together with this material we find cells in a more or less degenerated state, and fragments of the same, in conjunction with deformed free nuclei, still capable of taking the basic stains. In some places we find hyaline masses, true casts, filling the lumen. In preparations stained after Marchi, Golgi, or Weigert we find here and there fine fatty granules or droplets of varying size. This is by no means always the case, for we find many tubules in an advanced state of degeneration without signs of the fatty reactions. We have not been able to find the colloid bodies and crystals described by Councilman. The epithelial lining of the convoluted tubules is intensely degenerated, in the shape of cloudy swelling or fatty change. Osmic-acid preparations, stained by safranin and carmine, will show cells infiltrated with fat, and still presenting complete integrity of the nucleus. Mitotic figures are rare. We find also the special form of necrosis described by Councilman, namely, minute, rounded, or irregular bodies, well differentiated from the protoplasm. They stain intensely with eosin, and should be studied with high powers. The straight collecting tubes, the descending loop of Henle, the excretory ducts are less affected. Here the integrity of the epithelium is better preserved, and the form of degeneration most frequently encountered is the cloudy swelling. The tubes in the pyramids are often obstructed with cylinders corresponding with those that are found in the urine. The interstitial connective tissue also participates in the process. We find recent round-cell infiltrations around the glomerules (periglomerulitis), and about the cortical and medullary tubules. In some sections the infiltration is such as to invade the tubules themselves. The epithelial cells are found degenerated and compressed among connective-tissue cells of new formation and leucocytes.

Twice we have met with small abscesses of the kidney at the line of contact of cortical and medullary portions. Bearing upon the question of secondary infections we should state that one of these cases was of short duration.

The renal vessels are at times dilated, especially the larger ones, the interlobular and arciform; but no appreciable changes are found in the walls of these or of the smallest vessels. Hemorrhages are rarely met with.

We may classify the renal process in yellow fever as a hæmatogenous acute parenchymatous nephritis.

The Stomach.—The size of the organ is normal or slightly increased. On opening the viscus we find always more or less of a dark fluid, resembling coffee infusions of variable density. Frequently we find remnants of food, and at times fine shreds of mucous membrane. The spectroscopic, chemical, and microscopic investigations show that the coloring matter of this fluid is hæmoglobin or some one of its derivatives. The mucous membrane presents a reddish-gray color and ecchymotic points especially about the cardia and pylorus. The remainder of the surface presents also reddish points corresponding with the dilated vessels.

Histology.—The changes found vary in different cases. Sometimes they are limited, in the mucosa, to a simple congestion, specially characterized by a distention of the intertubular vessels that empty into the veins of the submucosa. In these cases only the superficial part of the mucosa is altered. The nucleus and the protoplasm do not take the stain well, but the epithelium is generally preserved. Such losses of it as may be encountered are to be ascribed to cadaveric changes. We find in these stomachs small superficial hemorrhagic foci, and at times small extravasations, but without any evidence that the capillaries have suffered in their integrity. Over the places just described the more superficial layers of the epithelium are degenerated, and the cells are found mixed in a magma composed of exfoliated cells, altered red globules, and free pigment. Other cases present deeper lesions. These are more pronounced toward the fundus and pylorus, especially the former. The chief or central cells of the glands present lesions that are characterized by lack of affinity with the hæmatoxylin, and a granular condition of the protoplasm; but we have not been able to demonstrate the presence of fat. These alterations do not generally affect uniformly the whole length of the gland. In the glandulæ propriæ of Kölliker we find normal chief cells alongside others more or less degenerated. The fundus of the gland is generally less affected than the periphery. In these cases the interstitial connective tissue participates in the degenerative process. This tissue presents a certain degree of translucency, and a lack of definition of its elements. These alterations are more manifest in the superficial layers. These do not stain distinctly with the eosin or with the fuchsin in van Gieson's process. The elastic fibres cannot be easily distinguished. We have seen no evidence of active connective-tissue proliferation, such as is found in most of the forms of gastritis, specially the hemorrhagic. We do find accumulations of round cells in the mucosa and submucosa, but without evidences of degeneration or active proliferation. The submucosa presents small areas of degeneration in the muscularis mucosæ. We have not been able to discover the punctated appearance described by Couto and Soudré. The vessels are often dilated, but no alterations can be found in their walls. The lumen is generally packed with red cells and a few leucocytes. In one case connective-tissue

elements of new formation were found infiltrating the submucosa about the veins, but even here no change could be demonstrated in the vascular wall. The muscular coat is normal in volume and shows no signs of degeneration. Distended vessels are seen among the layers of the musculature. The fat of the subserosa is not increased, nor is this membrane in any way altered.

The Intestines.—The lesions vary with the form and intensity of the infection. In those cases in which there have been intestinal hemorrhages the lesions are more intense. Invaginations of the small intestines have been met with. In one of our cases there were two such dislocations: one, at 1.5 metre from the duodenum, and the other 30 cm. lower down. There were no adhesions nor inflammatory exudate upon the serosa, but simply a congestion of the invaginated portion of the intestine.

On opening the intestine we find the color to be normal, except at some places where a reddish and cyanotic discoloration is apparent. This is more marked in the upper part of the intestine. Peyer's patches are not swollen or ulcerated. Histologically we find no serious lesions of the mucosa. It is less congested than that of the stomach. In most of our preparations there are marked cadaveric lesions, specially toward the duodenum. The epithelium covering the villi may be wanting or macerated, but it is generally present. The glands of Lieberkühn show no evidences of catarrhal inflammation, and the cells of the glands of Brunner present nothing abnormal. We find no abnormal round-cell or leucocytic infiltration. In hemorrhagic cases we find foci similar to those described in the stomach. The submucosa and the serosa are normal.

The large intestines are usually not affected. When we meet with lesions they are generally encountered in the lower portions of the gut and are catarrhal in character. The rectum generally contains fæcal matter, the consistence of which varies considerably. Hemorrhagic lesions are occasionally met with.

The Liver.—The volume of the organ is normal or slightly augmented. In 60 autopsies performed by Couto and Soudré the weight averaged 1,680 gm. The minimum was 1,200 and the maximum 2,200 gm. In 8 cases it varied between 1,400 and 1,500. Thirteen cases, investigated by Dr. Araujo Vianna, gave a specific weight as follows:

Absolute weight.	Specific weight.	Weight of the fat extracted by ether.	Absolute weight.	Specific weight.	Weight of the fat extracted by ether.
1900	1.045	226	1575	1.054	283
1610	1.037	236	1200	1.048	192
1500	1.079	185	1650	1.058	203
1750	1.071	233	1760	1.037	369
1915	1.052	204	1400	1.083	56
1770	1.022	306	1450	1.085	43
1800	1.028	420			

Color.—The color of the organ is characteristic of the disease. It may be compared with new leather or boxwood. Minute reddish points are generally found on the inferior surface. On section we observe the same discoloration, and we notice some reddish-gray points corresponding to portal spaces. The gall bladder usually contains small quantities of bile of dark color and syrupy consistence. The biliary passages are patulous, and on compression of the gall bladder the bile flows freely into the duodenum.

Histology.—From the study of our cases we conclude that the liver is the organ most seriously affected in yellow fever. We are at once struck by the deformity and disorder that prevail in the hepatic lobule. The cells are not radially distributed around the central vein, and the vascular net appears more tortuous than normally. Foreign elements, such as leucocytes and connective tissue of new formation, among the hepatic cells, give rise to this disorder. The protoplasm of the cells is more granular than normally, and presents vacuoles of varying size. These gradually gain upon the protoplasm until they invade it totally. Highly refractive hyaline bodies, more or less rounded generally, but at times presenting slight prolongations, are found in the cells and between them. These bodies take the eosin stain intensely, and take an orange color by the van Gieson method. According to Councilman they represent a partial necrosis that is characteristic of the acute fatty degenerations of the liver. ("Report of the Etiology and Prevention of Yellow Fever," by George M. Sternberg. "Report of the United States Marine Hospital Service," 1890.) The nucleus, usually excentric, generally stains well with the basic colors. This integrity of the nucleus contrasts in a remarkable manner with the disintegration of the protoplasm, and probably explains the rapid recuperation of the functional activity. Some nuclei are degenerated, as evidenced by signs of caryorrhexis and vacuolization. This occurs especially in the neighborhood of the portal spaces. Here also we meet occasionally with evidences of proliferation: double nuclei, various manifestations of mitosis, and small hepatic cells. In preparations colored by the Marchi method, or fixed in Flemming's fluid, we find that the vacuolizations of the protoplasm represent simply fat globules. These take the black color with the osmic acid. Their number varies from two to four, or they may run together, occupying the whole body of the cell. We rarely find necrotic areas. In one case the necrotic areas were confined to the periphery of the lobule, while the central portion, charged with fat, presented a normal coloration of the nuclei.

The interstitial connective tissue participates actively in the pathologic process. This is especially true in the portal spaces, where we encounter accumulations of round cells gathered around the blood-vessels and bile-ducts, and frequently pressing upon the latter and obliterating their lumen. This obliteration is not constant, for we meet with open ducts even in the midst of the proliferated connective tissue. In the interior of the acini we find also a considerable number of round and fusiform cells, together with fibrillæ of connective tissue and a few leucocytes.

It is a remarkable fact that we meet nowhere with evidences of a decided pigmentation of the organ. The free pigment is relatively scarce. It is manifested by a finely punctated appearance, and does not give the iron reactions. Pigment is also found within the cells. The scantiness of pigment in the yellow-fever liver is in strong contrast with the findings in other forms of jaundice. The walls of the biliary passages are normal.

The blood-vessels of the liver present no alteration of the walls. Their lumen is not distended, and in their contents we find but rarely an increase of the leucocytes. Hemorrhages are very rare.

The Pancreas.—In the few cases in which we have studied this gland we have found only cadaveric changes. We could not demonstrate the existence of the fatty degeneration described by some observers.

The Nervous System.—The meninges are generally in a normal condition. Sometimes ecchymotic spots are found in the dura. The sinuses are generally found filled with blood in those individuals who die in a comatose state. The arachnoid, the pia, and the choroid plexus are congested, and occasionally we meet with small extravasations. On section the blood flows somewhat freely from the vessels. The ventricles are dilated. Their walls, as well as the cerebro-spinal fluid, are slightly stained yellow. The brain is of normal consistence, but somewhat softened in prolonged cases. On section the color is normal and the punctated appearance is rather prominent. The spinal cord presents similar appearances with less prominence of congestive signs. The histology of the nervous system has not been carefully investigated.

Treatment. — The mortality statistics, referred to under the head of Prognosis (and they correspond with others from various sources) show the importance of early treatment in yellow fever. Not that we possess any specific that should be applied during the first hours of the disease, but that those patients are more likely to recover

who are put to bed at once, and who are kept on an absolute diet. Nothing else, if we except the administration of a laxative and the employment of some palliative measures, was done for the patients admitted to Las Animas and the Mercedes hospitals during the first two days of the disease. The results compare very favorably with those obtained without the proper sick-room discipline, and with active medication. I recommend in this connection the reading of a paper entitled "Notes on the Treatment of Yellow Fever at Las Animas Hospital," by Col. W. C. Gorgas, in the *Journal of the Association of Military Surgeons*, for October, 1903.

The patient should be put to bed at once and kept in the horizontal position. Clean linen for the bed and person should be furnished plentifully. Windows and doors should be left open (screened against mosquitoes, of course), care being taken to avoid only the direct action of strong currents of air. The quarters should be as clean as possible. Patients seem to do well when treated in tents, whereas the mortality is generally high in old yellow-fever hospitals. The skin should be cleansed and rubbed with hot water and soap, and clean, loose garments should be substituted for the clothing worn by the patient. It is not unreasonable to believe that these measures may lessen the chances of secondary infections. At any rate, the patients so treated do better than others.

A mild purgative—calomel and jalap or castor oil is ordered, and water is given freely through a drinking tube or feeding cup. From fifty to eighty ounces of fluid are given in the twenty-four hours. Plain water, pleasant alkaline waters, ginger ale, lemonade, orange leaf tea, are given, preferably cold, though some patients call for warm drinks. Weak solutions of bicarbonate of sodium may take the place of mineral waters. The patient is not allowed to sit up to empty the bladder and rectum.

Absolutely no drugs are given until we see clear indications for them, a condition that is not likely to arise in a large number of cases, or only from the third day onward in the grave cases. During this interval much can be done to relieve the sufferings of the patient and to gain his confidence.

External applications should be freely used: light sinapisms to the back of the neck, to the calves of the legs, to the loins, or to the epigastrium; ice caps to the head or to the back of the neck; rubbing of the legs or back with alcohol or some liniment; warm applications over the bladder if there be retention of urine; sedative water to the forehead. If the body-temperature be very high the surface should be sponged with cool water and alcohol, or an enema of cold water may be given.

If by night time the patient be suffering much from pains in the back and head, a dose of five grains of phenacetin may be given, and repeated, if necessary, once during the night. After the third night this drug is scarcely called for, and its use is probably harmful.

The first symptom that is likely to call for special treatment is vomiting. If the bowels have not acted since the initial purge we should now give a Seidlitz powder in broken doses, or effervescing magnesia, or calomel in minute, often repeated doses. If the vomiting does not stop readily, we should discontinue the administration of liquids by the mouth, and allow nothing but cracked ice in small quantities. At the same time rectal injections of warm physiologic salt solution in doses of six ounces every four hours should be prescribed. It is to be hoped now that the rectum has not been made irritable by the excessive use of purgatives, for much depends upon the continued administration of these injections perhaps for several days. When we have reached the fifth or sixth day of the disease, the question of feeding these patients presents itself. If there has been no vomiting one ounce of milk may be given every two hours by the mouth; but if we have been forced to use the rectal injections, two or three ounces of milk should be injected with the salt solution.

If the vomiting and retching be very frequent, a few doses of cocaine in tablet form should be tried, or ice may be applied to the throat. The oft-repeated vomiting is almost sure to lead to hemorrhage. Immediately upon the first appearance of brown flakes in the vomitus I prescribe tincture of the chloride of iron in five-drop doses every two hours. I give it usually with a little glycerin and lemon juice. The iron almost always reduces the frequency of the vomiting. I have tried adrenal extracts without success. If there be much hemorrhage from the mouth I prefer to use a mouth wash containing antipyrin. Wherever the source of the hemorrhage may be, I think the iron should be insisted upon.

The remainder of the treatment reduces itself to sustaining the strength of the patient, and stimulating the action of the heart and kidneys by the judicious use of strychnine and digitalis and alcohol; the two former by the hypodermic method, and the latter by the mouth or rectum. Alcohol is not well borne in large doses; a tablespoonful of champagne or some whiskey in carbonic-acid water, given occasionally when symptoms of collapse appear, is without doubt useful. Hypodermics of strychnine, or of digitalin in doses of gr. $\frac{1}{60}$ or gr. $\frac{1}{120}$ may be given every six hours with advantage. I do not believe these patients will stand as much strychnine as those suffering from other infectious diseases.

Digitalis is more specially indicated when the kidneys are inactive. In suppression of urine cold-water rectal injections have been recommended, and in some few cases I think I have done good through the diuretic action of calomel.

The prolonged typhoid cases, generally marked by intense jaundice, require alcohol and strychnine. Most of them have to take iron for a few days on account of the hemorrhages; but, as these subside, I think they are benefited by the use of small doses of chlorate of potassium. Later on, in the period of convalescence, they should take muriatic acid and nux vomica.

As already mentioned, about the fifth day we should begin to give milk, with lime water, if necessary. The dose should be gradually increased, and about the ninth day a mild solid diet may be ordered. Ice cream is much relished, and may be given before this.

The patient should be allowed to get on his feet gradually, and in the majority of cases he is up and about at the end of the second week. Very mild cases will have recovered completely in ten days, while others will require the use of peptonized food, tonics, and massage for a few days.

Prophylaxis.—The perfect success of the prophylactic measures against yellow fever is based on the complete knowledge we now possess of the mode of propagation of the disease. It is transmitted by the Stegomyia fasciata; the insect becomes *infected* by biting the yellow-fever patient at any time during the first three days of the disease; the insect becomes *infecting* twelve days after it has bitten the yellow-fever patient. The application of this knowledge to prophylactic practice is perfectly feasible.

The patient should be treated, if possible, within an enclosure known to be free from the Stegomyia mosquito. In cities exposed to the introduction of yellow fever there should be kept always in readiness such an enclosure—a mosquito-proof ward. In the city of Havana we have no hesitation in receiving cases of yellow fever from the shipping. We have, almost forcibly and with the idea of protecting the ship and the port to which it was bound, removed such a patient from a vessel and brought him into the city. Our security in this city depends simply on our having such an enclosure. The patient is brought under a mosquito bar to the mosquito-proof wards of Las Animas Hospital, where he is cared for by attendants, many of whom are non-immunes. This has been done now for three consecutive summers without a single instance of propagation of the disease.

If the patient must be treated at home steps should be taken to screen the windows and doors. If possible a room should be first fumigated to destroy the mosquitoes, and screened before the patient is brought into the apartment.

It is apparent that the source of infection, the patient, is quite under our control in most instances. Of course the possibility always exists of mild ambulatory cases that may escape our observation. I have always thought that such cases, specially among the negroes, are responsible for the spread of some epidemics.

If the patient has had the opportunity to infect mosquitoes before he comes under observation, it becomes necessary to destroy the infected insects. Here, again, we observe how completely this disease is under our control. The insects give us time to act. They can do no harm before the lapse of twelve days. Furthermore the Stegomyia mosquito is a domestic insect. It is not likely to migrate far from the patient. It will remain in the same room or at least in the same house. If the patient's quarters are protected against the smoke, the other parts of the building may be fumigated with pyrethrum. The houses immediately adjoining should be fumigated at the same time. After the recovery or death of the patient the room occupied by him should also be fumigated.

Although the pyrethrum is not so certain an insecticide as are certain other substances, it is more manageable, and can be applied in all places and at all times. If care be taken, during fumigation, to leave a sheet of paper, wet with mucilage, under a glass window, or under some opening pasted over with paper, the insects are sure to fly to the light, and will drop, when paralyzed, upon the paper beneath. In this manner, and by carefully sweeping the room, before freely opening the windows, after fumigating for four hours, we are quite sure of collecting all the mosquitoes. These should be burnt at once, or placed in a bottle, if we desire to determine the kind of insects found in the premises.

The complete success attained in Havana by these methods was in part due to the fact that most of the patients affected with yellow fever were hospital patients; that is, they could be removed at once to Las Animas, or to some of the private hospitals in which the sanitary department had seen to the preparation of adequate wards.

A fine was imposed on the physician who failed to report a case of yellow fever, and a commission of experts, whose opinion as to the diagnosis was final, visited the patient at once, and reported upon the nature of the disease. Preventive measures already instituted were continued or not according to the finding of the commission.

At the same time that these direct measures of prophylaxis are being carried out, every effort should be made to diminish the number of the Stegomyia mosquitoes in the locality. Deposits of water of all kinds should be reduced to a minimum. Waste waters, sinks, and pools should be frequently oiled with petroleum, and water barrels, tanks, and cisterns should be screened.

The above simple method of prophylaxis is based on the well-known studies of Dr. Finlay, and Drs. Reed, Carroll, Lazear, and Agramonte. These authors had left undetermined the duration of the period of infectivity of cases of yellow fever. From their experience and my own it appeared probable that this period of infectivity was limited to the first three days of the disease. In the report of the French commission (Marchoux, Salimbeni, Simond) sent to Rio by the Pasteur Institute, we find (*Annales de l'Institut Pasteur*, November, 1903) that special attention was paid to this point, and that inoculation experiments were made to show that a case of yellow fever on the fourth day was not capable of transmitting the disease.

Other experiments of the said commission are of interest from the point of view of individual prophylaxis, although I do not believe that they are capable of extensive practical application. Our system of general prophylaxis is so complete, the results are so certain, that we can scarcely believe that methods of individual prophylaxis will ever be called for.

The experimenters of the French commission have immunized individuals by injecting serum of yellow-fever patients previously treated by heating for five minutes at a temperature of 55° C., or by keeping it under a layer of vaseline during eight days. Dr. Carroll had already suggested the attenuation of the virus by heat. The commission also show that the serum of convalescents possesses preventive properties, and perhaps curative properties, as suggested by Finlay.

Juan Guiteras.

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